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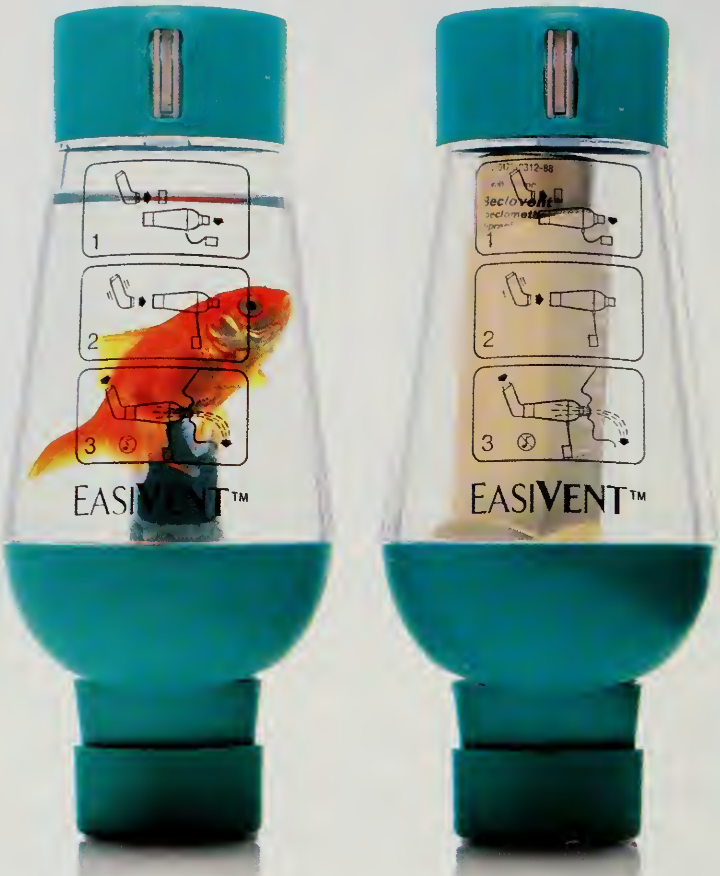

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The Cuffed Oropharyngeal Airway, a Novel Adjunct to the Management of Difficult Airways—Uezono S, Goto T, Nakata Y, Ichinose F, Niimi Y, Morita S. Anesthesiology 1998;88(6):1677–1679.

Use of the Laryngeal Mask Airway in Laboratory Cats—Asai T, Murao K, Katoh T, Shingu K. Anesthesiology 1998;88(6):1680–1682.

Is There Light at the End of the Tunnel?—Durbin CG Jr. Crit Care Med 1998;26(8):1303–1304.

A Subject of Ongoing Investigation: Can Exogenous Surfactant Be Used To Treat ARDS?—Serna D, Brenner M, Chen JC. Crit Care Med 1998;26(8):1307–1308.

Permanent Effects of Maternal Smoking on Offsprings' Lung Function (letter)—Upton MN, Watt GC, Davey Smith G, McConnachie A, Hart CL. Lancet 1998;352(9126):453.

Fenoterol and Asthma Mortality (letter)—Kremer G, Disse B. Lancet 1998;352(9126):485–486.

Anthrax as a Potential Biological Warfare Agent—Pile JC, Malone JD, Eitzen EM, Friedlander AM. Arch Intern Med 1998;158(5):429.

Anthrax is a zoonotic illness recognized since antiquity. Today, human anthrax has been all but eradicated from the industrialized world, with the vast majority of practitioners in the United States unlikely to have seen a case. Unfortunately, the disease remains endemic in many areas of the world, and anthrax poses a threat as a mass casualty-producing weapon if used in a biological warfare capacity.

Rapidly Progressive Extensive Subcutaneous Emphysema Associated with an Implantable Intratracheal Oxygen Catheter—Blackmon GM, Johnson MC 2nd, Plotkin E. Chest 1998;113(3):834.

Localized subcutaneous emphysema is a recognized complication of transtracheal oxygen catheters. It usually occurs in the immediate postoperative period or in association with catheter tip migration. This is a case of rapidly progressive, extensive subcutaneous emphysema apparently resulting from paroxysms of coughing in a patient with a normally functioning implanted intratracheal oxygen catheter several weeks after placement.

Does Evidence-Based Medicine Help the Development of Clinical Practice Guidelines?—Heffner JE. Chest 1998;113(3 Suppl):172S.

Formal methods for the development of clinical practice guidelines have emerged to address societal needs to decrease physician practice variation, slow the rise of health-care costs, monitor inappropriate care, assist clinicians to stay abreast of new clinical information, set research priorities, and promote better health-care outcomes. Evidence-based methods ensure that guidelines provide valid recommendations based on a critical appraisal of the best available evidence rather than informal, opinion-based processes.

Sustained Submaximal Exercise Does Not Alter the Integrity of the Lung Blood-Gas Barrier in Elite Athletes—Hopkins SR, Schoene RB, Henderson WR, Spragg RG, West JB. J Appl Physiol 1998;84(4):1185.

The extreme thinness of the pulmonary blood-gas barrier results in high mechanical stresses in the capillary wall when the capillary pressure rises during exercise. We have previously shown that, in elite cyclists, 6–8 min of maximal exercise increase blood-gas barrier permeability and result in higher concentrations of red blood cells, total protein, and leukotriene B4 in bronchoalveolar lavage (BAL) fluid compared with results in sedentary controls. To test the hypothesis that stress failure of the barrier only occurs at the highest level of exercise, we performed BAL in six healthy athletes after 1 h of exercise at 77% of maximal O_2 consumption. Controls were eight normal nonathletes who did not exercise before BAL. In contrast with our previous study, we did not find higher concentrations of red blood cells, total protein, and leukotriene B4 in the exercising athletes compared with control subjects. However, higher concentrations of surfactant apoprotein A and a higher surfactant apoprotein A-to-phospholipid ratio were observed in the athletes performing prolonged exercise, compared with both the controls and the athletes from our previous study. These results suggest that, in elite athletes, the integrity of the blood-gas barrier is altered only at extreme levels of exercise.

Mainstream End-Tidal Carbon Dioxide Monitoring in the Neonatal Intensive Care Unit—Rozycki HJ, Sysyn GD, Marshall MK, Malloy R, Wiswell TE. Pediatrics 1998;101(4 Pt 1):648.

BACKGROUND: Continuous noninvasive monitoring of arterial carbon dioxide (CO_2) in neonatal intensive care unit (NICU) patients would help clinicians avoid complications of hypocarbia and hypercarbia. End-tidal CO_2 monitoring has not been used in this population to date, but recent technical advances and the introduction of surfactant therapy, which improves ventilation-perfusion matching, might improve the clinical utility of end-tidal monitoring. OBJECTIVE: To determine the accuracy and precision of end-tidal CO_2 monitoring in NICU patients. DESIGN: Nonrandomized recording of simultaneous end-tidal and arterial CO_2 pairs. SETTING: Two university NICUs. PATIENTS: Forty-five newborn infants receiving mechanical ventilation who had indwelling arterial access, and a predefined subsample of infants who were <1000 g birth weight, <8 days of age, and who received surfactant therapy (extremely low birth weight -ELBW- <8). OUTCOME MEASURES: The correlation coefficient, degree of bias, and 95% confidence interval were determined for both the overall population and the ELBW <8 subgroup. Those factors which significantly influenced the bias were identified. The ability of the end-tidal monitor to alert the clinician to instances of hypocarbia or hypercarbia was determined. RESULTS: There were 411 end-tidal/arterial pairs analyzed from 45 patients. The correlation coefficient was 0.833 and the bias was -6. 9 mm Hg (95% confidence interval, ±11.5 mm Hg). The results did not differ markedly in the ELBW <8 infants. Measures of the degree of lung disease, the ventilation index and the oxygenation index, had small influences on the degree of bias. This type of capnometry identified 91% of the instances when the arterial CO_2 pressure was between 34 and 54 mm Hg using an end-tidal range of 29 to 45 mm Hg. End-tidal values outside this range had a 63% accuracy in predicting hypocarbia or hypercarbia. CONCLUSION: End-tidal CO_2 monitoring in NICU patients is as accurate as capillary or transcutaneous monitoring but less precise than the latter. It may be useful for trending or for screening patients for abnormal arterial CO_2 values.

Use of Medical Informatics To Implement and Develop Clinical Practice Guidelines—Owens DK. West J Med 1998;168(3):166.

Clinical practice guidelines have enormous potential to improve the quality of and accountability in health care. Making the most of this potential should become easier as guideline developers integrate guidelines within information systems and electronic medical records. A major barrier to such integration is the lack of computing infrastructure in many clinical settings. To successfully implement guidelines in information systems, developers must create more specific recommendations than those that have been required for traditional guidelines. Using reusable software components to create guidelines can make the development of protocols faster and less expensive. In addition, using decision models to produce guidelines enables developers to structure guideline problems systematically, to prioritize information acquisition, to develop site-specific guidelines, and to evaluate the cost-effectiveness of the explicit incorporation of patient preferences into guideline recommendations. Ongoing research provides a foundation for the use of guideline development tools that can help developers tailor guidelines appropriately to their practice settings. This article explores how medical informatics can help clinicians find, use, and create practice guidelines.

Effects of Inhaled Nitric Oxide in Patients with Acute Respiratory Distress Syndrome: Results of a Randomized Phase II Trial. Inhaled Nitric Oxide in ARDS Study Group—Dellinger RP, Zimmerman JL, Taylor RW, Straube RC, Hauser DL, Criner GJ, et al. Crit Care Med 1998;26(1):15.

OBJECTIVES: To evaluate the safety and physiologic response of inhaled nitric oxide (NO) in patients with acute respiratory distress syndrome (ARDS). In addition, the effect of various doses of inhaled NO on clinical outcome parameters was assessed. DESIGN: Prospective, multicenter, randomized, double-blind, placebo-controlled study. SETTING: Intensive care units of 30 academic, teaching, and community hospitals in the United States. PATIENTS: Patients with ARDS, as defined by the American-European Consensus Conference, were enrolled into the study if the onset of disease was within 72 h of randomization. INTERVENTIONS: Patients were randomized to receive placebo (nitrogen gas) or inhaled NO at concentrations of 1.25, 5, 20, 40, or 80 ppm. MEASUREMENTS & MAIN RESULTS: Acute increases in P_{aO_2}, decreases in mean pulmonary arterial pressure, intensity of mechanical ventilation, and oxygenation index were examined. Clinical outcomes examined were the dose effects of inhaled NO on mortality, the number of days alive and off mechanical ventilation, and the number of days alive after meeting oxygenation criteria for extubation. A total of 177 patients were enrolled over a 14-month period. An acute response to treatment gas, defined as a P_{aO_2} increase ≥ 20%, was seen in 60% of the patients receiving inhaled NO with no significant differences between dose groups. Twenty-four percent of placebo patients also had an acute response to treatment gas during the first 4 hrs. The initial increase in oxygenation translated into a reduction in the F_{IO_2} over the first day and in the intensity of mechanical ventilation over the first 4 days of treatment, as measured by the oxygenation index. There were no differences among the pooled inhaled NO groups and placebo with respect to mortality rate, the number of days alive and off mechanical ventilation, or the number of days alive after meeting oxygenation criteria for extubation. However, patients receiving 5 ppm inhaled NO showed an improvement in these parameters. In this dose group, the percentage of patients alive and off mechanical ventilation at day 28 (a post hoc analysis) was higher (62% vs 44%) than the placebo group. There was no apparent difference in the number or type of adverse events reported among those patients receiving inhaled NO compared with placebo. Four patients had methemoglobin concentrations > 5%. The mean inspired nitrogen dioxide concentration in inhaled NO patients was 1.5 ppm. CONCLUSIONS: From this placebo-controlled study, inhaled NO appears to be well tolerated in the population of ARDS patients studied. With mechanical ventilation held constant, inhaled NO is associated with a significant improvement in oxygenation compared with placebo over the first 4 h of treatment. An improvement in oxygenation index was observed over the first 4 days. Larger phase III studies are needed to ascertain if these acute physiologic improvements can lead to altered clinical outcome.

Aerosolized Antibiotics in Mechanically Ventilated Patients: Delivery and Response—Palmer LB, Smaldone GC, Simon SR, O'Riordan TG, Cuccia A. Crit Care Med 1998;26(1):31.

OBJECTIVES: To determine whether aerosolized antibiotics can be delivered efficiently to the lower respiratory tract in mechanically ventilated patients and to define possible clinical

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responses to these agents. DESIGN: Prospective serial study with cases as their own control. SETTING: A 10-bed respiratory care unit for patients with chronic respiratory failure in a tertiary university hospital. PATIENTS: Ventilator dependent patients who are otherwise medically stable. All subjects had a tracheostomy in place, were colonized with gram-negative organisms, and produced purulent secretions which could be sampled daily. INTERVENTIONS: Six patients received 9 courses of nebulized therapy, which consisted of treatments every 8 h of gentamicin (80 mg) or amikacin (400 mg) for 14 to 21 days. MEASUREMENTS & MAIN RESULTS: Doses to the lung were measured using radiolabeled aerosols and antibiotic concentrations in sputum. The response was assessed by a) changes in the volume of respiratory secretions; b) effect on bacterial cultures; and c) changes in the inflammatory cells and mediators of inflammation of the respiratory secretions (interleukin-1beta [IL-1beta], tumor necrosis factor-alpha [TNF-alpha], soluble intercellular adhesion molecule-1 [sICAM-1], and human leukocyte elastase). On average, patients inhaled 35.4 ± 5.08% (SD) of the initial drug placed in the nebulizer (neb-charge). Of this neb-charge, 9.50 ± 2.78% was found on the respirator tubing and tracheostomy tube and 21.9 ± 7.15% was actually deposited in the lungs. The remainder of the neb-charge was sequestered in the nebulizer or exhaled. Trough sputum concentrations averaged 4.3 ± 3.2 μg/mL/mg neb-charge (range 234 to 520 μg/mL) and increased to 16.6 ± 8.1 μg/mL/mg neb-charge (range 1005 to 5839 μg/mL) immediately after therapy ($p = 0.011$). Serum concentrations were undetectable in most determinations except for a single patient who was in renal failure (8.7 μg/mL amikacin). Treatment caused a significant reduction in the volume of secretions ($p = 0.002$). Weekly cultures revealed eradication of Pseudomonas species, *Serratia marcescens*, and *Enterobacter aerogenes* in most of the trials. Before antibiotic treatment, concentrations of IL-1beta were higher than those reported in acute respiratory distress syndrome. Throughout the duration of the study, IL-1beta correlated significantly with the absolute number of macrophages, neutrophils, and lymphocytes, respectively ($r2 = 0.55$, $p = 0.002$; $r2 = 0.50$, $p < 0.0004$, $r2 = 0.36$, $p = 0.005$). TNF-alpha concentrations correlated with lymphocytes and neutrophils, respectively ($r2 = 0.27$, $p = 0.013$, $r2 = 0.21$, $p = 0.033$). sICAM-1 concentrations increased two-fold ($p < 0.001$) during treatment and then returned to baseline. The volume of secretions was related to neutrophil and IL-1β concentrations, respectively ($r2 = 0.25$, $p = 0.008$, $r2 = 0.35$, $p = 0.006$). CONCLUSIONS: Nebulizer delivery of aerosolized aminoglycosides is efficient and predictable. In our clinical model, aerosolized antibiotics can make a significant impact on respiratory secretions. Their efficacy in treatment of critically ill patients remains to be determined. *See the related editorial: **Aerosolized Antimicrobials: Another Look**. Itokazu GS, Weinstein RA. Crit Care Med 1998;26(1): 5–6.*

Confidence in Life-Support Decisions in the Intensive Care Unit: A Survey of Healthcare Workers. Canadian Critical Care Trials Group—Walter SD, Cook DJ, Guyatt GH, Spanier A, Jaeschke R, Todd TR, Streiner DL. Crit Care Med 1998;26(1):44.

OBJECTIVE: To examine the relationship between intensive care unit (ICU) healthcare workers' confidence and their decision to withdraw life support. DESIGN: Cross-sectional survey of Canadian intensivists, ICU housestaff, and bedside nurses. Respondents chose the level of care (from comfort measures only to full aggressive care) for 12 patients described in clinical scenarios, and rated their confidence in their decisions. SETTING: Thirty-seven Canadian university-affiliated hospitals. PATIENTS: None. INTERVENTIONS: We used discrete data analysis models to examine the association between the chosen level of care, confidence in the decisions, the clinical scenario, and healthcare worker group. MEASUREMENTS & MAIN RESULTS: The response rate was 1,361 (76%)/1,795; for this analysis, we used data from 1,306 respondents with completed questionnaires. Responses for each scenario varied widely among respondents. The level of care chosen was dependent on the scenario, the healthcare worker group, and the confidence with which the decisions were made ($p < 0.001$ for each). Intensivists were less aggressive than the ICU nurses, who were less aggressive than the housestaff, but the magnitude of effect was small. Overall, respondents were very confident about their decisions 34% of the time. After adjustment for clinical scenario and chosen level of care, intensivists were more confident than nurses, who were more confident than housestaff (40% of intensivists, 29% of nurses, and 23% of housestaff were very confident). In general, healthcare workers tended to be more confident when they chose extreme levels of care than when they chose intermediate levels of care. Considerable variability in responses to scenarios remained even when we considered only those responses made with the highest level of confidence. CONCLUSIONS: While confidence in decisions about withdrawal of life support increases with seniority and authority, consistency of decisions may not. When given standard information, healthcare workers can make contradictory decisions yet still be very confident about the level of care they would administer.

Acute Exacerbations of Chronic Obstructive Pulmonary Disease and Mechanical Ventilation: A Reevaluation—Moran JL, Green JV, Homan SD, Leeson RJ, Leppard PI. Crit Care Med 1998;26(1):71.

OBJECTIVE: To review the intensive care unit (ICU) experience of patients admitted with acute exacerbations of chronic obstructive pulmonary disease. DESIGN: Retrospective case series. SETTING: University teaching hospital. PATIENTS: We reviewed the records of 100 consecutive ICU admissions of patients with acute exacerbations of chronic obstructive pulmonary disease over a period of 4.25 yrs. INTERVENTIONS: None. MEASUREMENTS & MAIN RESULTS: Patients were characterized using a computerized prospective database and case note review. Multivariate analysis identified variables predicting ICU and hospital length of stay. The Cox proportional hazards model was used to analyze survival after hospital discharge. Seventy-five patients (24 female and 51 male, mean age 68.5 ± 7 [SD] y) with 100 ICU admissions were identified. Premorbid airway obstruction was severe, with forced expiratory volume in 1 sec (FEV$_1$)/forced vital capacity (FVC) of 0.7 ± 0.34 L and FEV$_1$/FVC of 39 ± 16%. Thirty-two percent received home-administered oxygen and 42% were housebound. The pre-ICU admission P_{aCO_2} was 86 ± 28 torr (11.5 ± 3.7 kPa), with a pH of 7.24 ± 0.11 and a P_{aO_2}/F_{IO_2} of 190 ± 66. ICU admission Acute Physiology and Chronic Health Evaluation II score was 18 ± 5. Forty-three patients were mechanically ventilated for a median of 4 days (range 0.08 to 30). Tracheostomy, in 7 patients, was maintained for 21 ± 7 days. Ventilation time and tracheostomy frequency predicted length of ICU stay (median 3 days; range 1 to 40) and hospital stay (17 days; 4 to 97), respectively. ICU and hospital case-fatality rates were 1% and 11%. Out-of-hospital (24-month) probability of survival was predicted by plasma albumin concentration at the time of ICU admission; this probability of survival was 0.64 at an albumin concentration of 38 g/L. CONCLUSIONS: ICU admission of severely ill chronic obstructive pulmonary disease patients results in acceptable outcomes. Survival of ≤ 2 yrs is not affected by mechanical ventilation or tracheostomy requirement.

Noninvasive Ventilation via Bilevel Positive Airway Pressure Support in Pediatric Practice—Padman R, Lawless ST, Kettrick RG. Crit Care Med 1998;26(1):71.

OBJECTIVE: To evaluate the efficacy of bilevel positive airway pressure support in critically ill children with underlying medical conditions. DESIGN: Prospective, clinical study. SETTING: Pediatric intensive care unit (ICU). PATIENTS: Thirty-four patients (6 mos to 20 y, mean 11.06 ± 0.9 y) with impending respiratory failure were enrolled in the study. All patients required airway or oxygenation/ventilation support (awake or asleep) and required admission to our pediatric ICU. Each patient served as his or her own control. Exclusion criteria were absent cough or gag reflex, multiple organ system failure, age of < 6 mos, vocal cord paralysis, and noncooperation with nasal mask. INTERVENTIONS: Bi-level positive airway pressure support ventilation. MEASUREMENTS & MAIN RESULTS: Thirty-four patients with 35 episodes of respiratory insufficiency requiring airway support or oxygenation/ventilatory support were treated with bi-level positive airway pressure support ventilation. Dyspnea score decreased at least 2 deviations in all patients; dyspnea score decreased 5 deviations in 67% of patients. Resting heart rate decreased from 126 ± 3.2 to 102 ± 3.2 beats/min ($p < 0.001$), respiratory rate decreased from 39 ± 3 to 25 ± 1 breaths/min ($p < 0.004$), bicarbonate concentrations decreased from 30.0 ± 1.0 to 24.0 ± 0.7 mmol/L ($p < 0.01$), and room air saturation increased from 85 ± 2% to 97 ± 1%. Bi-level positive airway pressure support ventilation failure was characterized by an inability to stabilize progression of respiratory failure and the subsequent placement of an artificial airway. Three patients required placement of an artificial airway. CONCLUSIONS: A decrease in respiratory rate, heart rate, and dyspnea score and an improvement in oxygenation were noted in $> 90\%$ of patients studied, resulting in only an 8% frequency of intubation. The efficacy of bi-level positive airway pressure support ventilation in selected groups of patients indicates the need to include this form of noninvasive pressure support ventilation in the care offered by pediatric ICUs.

Changes in Breathing Pattern and Respiratory Muscle Performance Parameters during Difficult Weaning—Capdevila X, Perrigault PF, Ramonatxo M, Roustan JP, Peray P, d'Athis F, Prefaut C. Crit Care Med 1998;26(1):79.

OBJECTIVE: This study examined, using noninvasive means, the changes in breathing pattern and inspiratory muscle pressure-time indices during difficult progressive withdrawal of pressure-support ventilation. DESIGN: A prospective analysis of the temporal evolution of several respiratory variables in difficult-to-wean patients. SETTING: A university hospital intensive care unit. PATIENTS: A heterogeneous group of 17 patients receiving prolonged mechanical ventilation. INTERVENTIONS: Daily measurements of breathing pattern and respiratory muscle performance parameters in difficult-to-wean patients. MEASUREMENTS & MAIN RESULTS: We examined breathing pattern variables, rapid shallow breathing (respiratory rate/tidal volume), tracheal occlusion pressure, maximal inspiratory pressure (PI_{max}), and the tension-time index of the inspiratory muscles ($TTmus = P(I)/P(I)max \times Ti/Ttot$) (where Ti/Ttot is inspiratory fraction of the cycle). All measurements were repeated at 24-hr intervals throughout the difficult weaning period. The patients were extubated on satisfying 10 of 12 classical weaning criteria. Eleven patients were successfully weaned from mechanical ventilation while 6 patients were not. Weaning failure was associated with the following: a) longer periods of mechanical ventilation before weaning; b) high values of tracheal occlusion pressure, respiratory rate, minute ventilation, and effective impedance maintained throughout the difficult weaning period; and c) persistent high P_{aCO_2} and intrinsic positive end-expiratory pressure values. As the weaning failure patients' inspiratory muscles confronted an increasing inspiratory load, values of the tension-time index of the inspiratory muscles entered or remained in the fatigue zone. In contrast, weaning success patients normalized their breathing pattern and decreased their tracheal occlusion pressure, effective impedance, and tension-time index values. CONCLUSIONS: Breathing pattern alterations and respiratory muscle performance impairments lead to ventilator dependency after prolonged mechanical ventilation. The measurement of variables such as the noninvasive tracheal occlusion pressure, inspiratory power of breathing, and tension-time index of the inspiratory muscles facilitate the management of difficult-to-wean patients.

Evaluation of Antismoking Advertising Campaigns—Goldman LK, Glantz SA. JAMA 1998; 279(10):772.

CONTEXT: Active and passive smoking are the first and third leading preventable causes of death. Many states are running or initiating antitobacco media campaigns. OBJECTIVE: To review research on the effectiveness of different antismoking messages and published evidence of the effectiveness of paid antismoking advertising. DATA SOURCES: Focus group studies conducted by professional advertising agencies that contract with California, Massachusetts, and Michigan to run their antismoking advertising campaigns, the Centers for Disease Control and Prevention's Media Campaign Resource Book, and copies of the advertisements. In total, we reviewed the results of 186 focus groups involving more than 1500 children and adults dealing with 118 advertisements that had actually been aired and additional concept advertisements that were not produced. Published literature was located using MEDLINE and standard bibliographic sources on the effectiveness of large, paid antitobacco media campaigns. We also reviewed reports and studies conducted by, or for, the California and Massachusetts health departments on program effectiveness, and conducted our own comparison of California vs Massachusetts using cigarette consumption data from the Tobacco Institute. STUDY SELECTION: All available studies. DATA SYNTHESIS: Eight advertising strategies to prevent people from starting to smoke and persuading them to stop were reviewed: industry manipulation, secondhand smoke, addiction, cessation, youth access, short-term effects, long-term health effects, and romantic rejection. These focus groups identified strategies that would be expected to be effective and ineffective. Regression analysis was used to compare the cost-effectiveness of the California and Massachusetts programs. CONCLUSIONS: Focus group participants indicated that industry manipulation and secondhand smoke are the most effective strategies for denormalizing smoking and reducing cigarette consumption. Addiction and cessation can be effective when used in conjunction with the industry manipulation and secondhand smoke strategies. Youth access, short-term effects, long-term health effects, and romantic rejection are not effective strategies. More aggressive advertising strategies appear to be more effective at reducing tobacco consumption.

Influence of Airway Management on Ventilator-Associated Pneumonia: Evidence from Randomized Trials—Cook D, De Jonghe B, Brochard L, Brun-Buisson C. JAMA 1998; 279(10):781.

OBJECTIVE: Ventilator-associated pneumonia (VAP) is a serious complication of critical illness, conferring increased morbidity and mortality. Many interventions have been studied to reduce the risk of VAP. We systematically reviewed the influence of airway management on VAP in critically ill patients. DATA SOURCES: Studies were identified through searching MEDLINE and EMBASE from 1980 through July 1997 and by searching SCISEARCH, the Cochrane Library, bibliographies of primary and review articles, personal files, and contact with authors of the randomized trials. STUDY SELECTION: We selected randomized trials evaluating ventilator circuit and secretion management strategies on the rate of VAP. DATA EXTRACTION: Two investigators independently abstracted key data on design features, the population, intervention, and outcome of the studies. DATA SYNTHESIS: The frequency of ventilator circuit changes and the type of endotracheal suction system do not appear to influence VAP rates (3 trials, none with significant difference; range of relative risks [RRs], 0.84–0.91). However, lower VAP rates may be associated with avoidance of heated humidifiers and use of heat and moisture exchangers (5 trials, only 1 showing a significant difference; range of RRs, 0.34–0.86), use of oral vs nasal intubation (1 trial; RR, 0.52; 95% confidence interval, 0.24–1.13), subglottic secretion drainage vs standard endotracheal tubes (2 trials, 1 showing a significant difference; range of RRs, 0.46–0.57), and kinetic vs conventional beds (5 trials, only 1 showing a significant difference; range of RRs, 0.35–0.78). CONCLUSIONS: Some ventilator circuit and secretion

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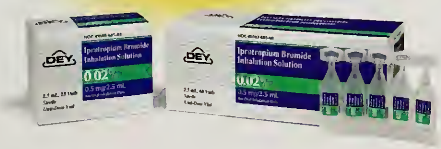

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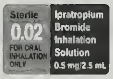

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WARNINGS: The use of Ipratropium Bromide Inhalation Solution as a single agent for the relief of bronchospasm in acute COPD exacerbation has not been adequately studied. Drugs with faster onset of action may be preferable as initial therapy in this situation. Combination of Ipratropium Bromide Inhalation Solution and beta agonists has not been shown to be more effective than either drug alone in reversing the bronchospasm associated with acute COPD exacerbation.

Immediate hypersensitivity reactions may occur after administration of ipratropium bromide, as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm and oropharyngeal edema.

PRECAUTIONS: General: Ipratropium bromide should be used with caution in patients with narrow angle glaucoma, prostatic hypertrophy or bladder neck obstruction.

Information for Patients: Patients should be advised that temporary blurring of vision, precipitation or worsening of narrow-angle glaucoma or eye pain may result if the solution comes into direct contact with the eyes. Use of a nebulizer with mouthpiece rather than face mask may be preferable, to reduce the likelihood of the nebulizer solution reaching the eyes. Patients should be advised that Ipratropium Bromide Inhalation Solution can be mixed in the nebulizer with albuterol or metaproterenol if used within one hour. Drug stability and safety of Ipratropium Bromide Inhalation Solution when mixed with other drugs in a nebulizer have not been established. Patients should be reminded that Ipratropium Bromide Inhalation Solution should be used consistently as prescribed throughout the course of therapy.

Drug Interactions: Ipratropium bromide has been shown to be a safe and effective bronchodilator when used in conjunction with beta adrenergic bronchodilators. Ipratropium bromide has also been used with other pulmonary medications, including methylxanthines and corticosteroids, without adverse drug interactions.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Two-year oral carcinogenicity studies in rats and mice have revealed no carcinogenic potential at dietary doses up to 6 mg/kg/day of ipratropium bromide.

Results of various mutagenicity studies (Ames test, mouse dominal lethal test, mouse micronucleus test and chromosome aberration of bone marrow in Chinese hamsters) were negative.

Fertility of male or female rats at oral doses up to 50 mg/kg/day was unaffected by ipratropium bromide administration. At doses above 90 mg/kg, increased resorption and decreased conception rates were observed.

Pregnancy: *TERATOGENIC EFFECTS:*
Pregnancy Category B. Oral reproduction studies performed in mice, rats and rabbits at doses of 10, 100, and 125 mg/kg respectively and inhalation reproduction studies in rats and rabbits at doses of 1.5 and 1.8 mg/kg (or approximately 38 and 45 times the recommended human daily dose) respectively, have demonstrated no evidence of teratogenic effects as a result of ipratropium bromide. However, no adequate or well controlled studies have been conducted in pregnant women. Because animal reproduction studies are not always predictive of human response, ipratropium bromide should be used during pregnancy only if clearly needed.

Nursing Mothers: It is not known whether ipratropium bromide is excreted in human milk. Although lipid-insoluble quaternary bases pass into breast milk, it is unlikely that ipratropium bromide would reach the infant to a significant extent, especially when taken by inhalation since ipratropium bromide is not well absorbed systemically after inhalation or oral administration. However, because many drugs are excreted in human milk, caution should be exercised when ipratropium bromide is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 12 have not been established.

ADVERSE REACTIONS: Adverse reaction information concerning Ipratropium Bromide Inhalation Solution is derived from 12-week active-controlled clinical trials. Additional information is derived from foreign post-marketing experience and the published literature.

All adverse events, regardless of drug relationship, reported by three percent or more patients in the 12-week controlled clinical trials appear in the table.

All Adverse Events, From a Double-blind, Parallel, 12-week Study of Patients with COPD*

	PERCENT OF PATIENTS				
	Ipratropium Bromide (500 mcg t.i.d.)	Meta-proterenol (15 mg t.i.d.)	Ipratropium / Bromide/ Metaproterenol (500 mcg t.i.d / 15 mg t.i.d.)	Albuterol (2.5 mg t.i.d.)	Ipratropium Bromide/ Albuterol (500 mcg t.i.d 2.5 mg t.i.d.)
	n = 219	n = 212	n = 108	n = 205	n = 100
Body as a Whole-General Disorders					
Headache	6.4	5.2	6.5	6.3	9.0
Pain	4.1	3.3	0.9	2.9	5.0
Influenza-like symptoms	3.7	4.7	6.5	0.5	1.0
Back Pain	3.2	1.9	1.9	2.4	0.0
Chest Pain	3.2	4.2	5.6	2.0	1.0
Cardiovascular Disorders					
Hypertension/ Hypertension Aggravated	0.9	1.9	0.9	1.5	4.0
Central & Peripheral Nervous System					
Dizziness	2.3	3.3	1.9	3.9	4.0
Insomnia	0.9	0.5	4.6	1.0	1.0
Tremor	0.9	7.1	8.3	1.0	0.0
Nervousness	0.5	4.7	6.5	1.0	1.0
Gastrointestinal System Disorders					
Mouth Dryness	3.2	0.0	1.9	2.0	3.0
Nausea	4.1	3.8	1.9	2.9	2.0
Constipation	0.9	0.0	3.7	1.0	1.0
Musculo-skeletal System Disorders					
Arthritis	0.9	1.4	0.9	0.5	3.0
Respiratory System Disorders (Lower)					
Coughing	4.6	8.0	6.5	5.4	6.0
Dyspnea	9.6	13.2	16.7	12.7	9.0
Bronchitis	14.6	24.5	15.7	16.6	20.0
Bronchospasm	2.3	2.8	4.6	5.4	5.0
Sputum Increased	1.4	1.4	4.6	3.4	0.0
Respiratory Disorder	0.0	6.1	6.5	2.0	4.0
Respiratory System Disorders (Upper)					
Upper Respiratory Tract Infection	13.2	11.3	9.3	12.2	16.0
Pharyngitis	3.7	4.2	5.6	2.9	4.0
Rhinitis	2.3	4.2	1.9	2.4	0.0
Sinusitis	2.3	2.8	0.9	5.4	4.0

*All adverse events, regardless of drug relationship, reported by the three percent or more patients in the 12-we controlled clinical trials

Additional adverse reactions reported in less than three percent of the patients treated with ipr tropium bromide include tachycardia, palpitations, eye pain, urinary retention, urinary tract infectio and urticaria. Cases of precipitation or worsening of narrow-angle glaucoma and acute eye pain hav been reported.

Lower respiratory adverse reactions (bronchitis, dyspnea and bronchospasm) were the most commo events leading to discontinuation of ipratropium bromide therapy in the 12-week trials. Headach mouth dryness and aggravation of COPD symptoms are more common when the total daily dose o ipratropium bromide equals or exceeds 2,000 mcg.

Allergic-type reactions such as skin rash, angioedema of tongue, lips and face, urticaria, lary gospasm and anaphylactic reaction have been reported. Many of the patients had a history allergies to other drugs and/or foods.

HOW SUPPLIED: Ipratropium Bromide Inhalation Solution is a clear, colorless solution supplied in a uni dose vial containing 2.5 mL. Supplied in cartons as listed below:

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management strategies may influence VAP rates in critically ill patients. Whether these strategies are adopted in practice depends on several factors such as the magnitude and precision of estimates of benefit and harm, as well as access, availability, and costs.

Continuous Jugular Bulb Venous Oxygen Saturation Validation and Variations during Intracranial Aneurysm Surgery—Clavier N, Schurando P, Raggueneau JL, Payen DM. J Crit Care 1997;12(3):112.

PURPOSE: During intracranial aneurysm surgery, numerous factors may alter cerebral blood flow and oxygen supply-demand balance. Continuous monitoring of jugular bulb venous oxygen saturation (S_{vjO_2}) may help in the anesthetic management of such procedures. MATERIALS & METHODS: Fiberoptic S_{vjO_2} was continuously monitored in 7 patients during intracranial aneurysm surgery. Fiberoptic S_{vjO_2} measurement was compared with IL3 CO-OXIMETER determination from 85 paired samples. The occurrence of large S_{vjO_2} variations (S_{vjO_2} variation reaching 10% or more of stable preceding value) during aneurysm surgery was recorded and classified according to the association or not with systemic clinical or therapeutic changes. RESULTS: Fiberoptic S_{vjO_2} showed a limited accuracy, with limits of agreement with IL3 CO-OXIMETER at -16.8% and +10.7% and a small bias (-3.1%). S_{vjO_2} variations were frequent during aneurysm surgery, ranging from 3 to 22% during procedures lasting 6 h (range 4.5 to 7). Half of these variations occurred in the absence of any systemic clinical or therapeutic change, most often leading to an increased S_{vjO_2}. CONCLUSIONS: Although the accuracy of fiberoptic S_{vjO_2} determination is limited, it allows the detection of cerebral blood flow and oxygen supply-demand imbalance during aneurysm surgery. The frequent occurrence of S_{vjO_2} elevations is suggestive of reactive hyperemia mechanisms.

Impact of Invasive and Noninvasive Quantitative Culture Sampling on Outcome of Ventilator-Associated Pneumonia: A Pilot Study—Sanchez-Nieto JM, Torres A, Garcia-Cordoba F, El-Ebiary M, Carrillo A, Ruiz J, et al. Am J Respir Crit Care Med 1998;157(2):371.

We performed an open, prospective, randomized clinical trial in 51 patients receiving mechanical ventilation for more than 72 h, in order to evaluate the impact of using either invasive (protected specimen brush [PSB] and bronchoalveolar lavage [BAL] via fiberoptic bronchoscopy) or noninvasive (quantitative endotracheal aspirates [QEA]) diagnostic methods on the morbidity and mortality of ventilator-associated pneumonia (VAP). Patients were randomly assigned to 2 groups: Group A patients (n = 24) underwent QEA, PSB, and BAL; Group B patients (n = 27) underwent only QEA cultures. Empiric antibiotic treatment was given according to the attending physician and was modified according to the results of cultures and sensitivity in Group A using PSB and BAL results and in Group B based upon QEA cultures. Bacteriologic cultures were done quantitatively for EA, PSB, and BAL. Thresholds of ≥ 10(5), ≥ 10(3), and ≥ 10(4) CFU/mL were used for QEA, PSB, and BAL, respectively. Microbial cultures from Group A patients were positive in 16 (67%) BAL samples, 14 (58%) PSB samples, and 16 (67%) QEA samples. In Group B patients, QEA microbial cultures yielded positive results in 20 of 27 (74%) samples. In Group A, there was total agreement between culture results of the 3 techniques on 17 (71%) occasions. In 5 (21%) cases, QEA coincided with either BAL or PBS. In only 2 (8%) cases, QEA cultures did not coincide with either PSB or BAL. No cases of positive BAL or PSB cultures had negative QEA cultures. Initial antibiotic treatment was modified in 10 (42%) patients from Group A and in 4 (16%) patients from Group B ($p < 0.05$). The observed crude mortality rate was 11 of 24 (46%) in Group A, and 7 of 27 (26%) in Group B, whereas the adjusted mortality rates (observed crude minus predicted at admission) for Groups A and B were 29 and 10%, respectively. There were no statistically significant differences when

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comparing crude and adjusted mortality rates of Groups A and B. There were no differences in mortality between both groups when comparing pneumonia, considering together *Pseudomonas aeruginosa* and *Acinetobacter spp.* (Group A, 33% versus Group B, 27%). There were no differences between Groups A and B with regard to ICU stay duration and total duration of mechanical ventilation. In this pilot study, the impact of bronchoscopy was to lead to more frequent antibiotic changes with no change in mortality. Further studies with larger population samples are warranted to confirm these findings. *See the related editorial:* ***Mortality and the Diagnosis of Ventilator-Associated Pneumonia: A new Direction.*** *Wunderink RG. Am J Respir Crit Care Med 1998;157(2): 349–350.*

Automatic Actuation of a Dry Powder Inhaler into a Nonelectrostatic Spacer—Bisgaard H. Am J Respir Crit Care Med 1998; 157(2):518.

This article describes a new "automatic spacer" device, which has been developed to improve the delivery of inhaled medication to young children. In the device, a dry powder inhaler (DPI) is mechanically actuated into a nonelectrostatic spacer, producing an aerosol cloud of fine drug particles (aerodynamic diameter, $< 4.7\ \mu m$) with a long half-life. The new device combines the principal advantages of the conventional spacer and the DPI. It has the potential to provide a high ratio between lung dose and pharyngeal dose, without need for coordination or forced inhalation, and it avoids exposure of the patient to the additives and propellants used in pressurized metered dose inhalers. Studies with the prototype device show a high yield of fine drug particles in the aerosol (mass median aerodynamic diameter, 2.8 μm), a high repeatability of drug delivery owing to the mechanical nature of the actuation (relative standard deviation, 12%), and a prolonged residence time of the fine particle aerosol (half-life of the fallout of the fine particles, 82 s). These features should prove advantageous in the treatment of young children with inhaled medication.

A Randomized Trial Comparing Peak Expiratory Flow and Symptom Self-Management Plans for Patients with Asthma Attending a Primary Care Clinic—Turner MO, Taylor D, Bennett R, Fitzgerald JM. Am J Respir Crit Care Med 1998;157(2):540.

Great emphasis is placed on educating asthmatics to use action plans to achieve better control of symptoms. The use of peak flow meters (PFM) has been recommended as an important part of self-management plans. We studied 92 (47 F) adult patients with asthma in a primary care setting to compare the effectiveness of action plans using either peak flow monitoring or symptoms to guide self-management. Each patient was instructed in the use of the action plan in the context of a 6-mo asthma education program taught by a nurse. Patients were already using inhaled corticosteroids or were newly prescribed corticosteroids by their family physician. Forty-four patients were randomized to the PFM group and 48 to the symptoms group. Spirometry, symptom scores, quality of life, medication use, and measures of health care utilization and morbidity (emergency department visits, hospitalizations, unscheduled doctor visits, and days lost from work or school) were recorded at baseline and throughout the study period. P_{C20} methacholine was measured at the first and at the final visits. There were significant improvements within groups for FEV_1, symptoms score, P_{C20} methacholine, and quality of life, but no between-group differences. A significant shift from higher to lower daily use of β-agonists ($p < 0.008$ for both groups) and significant shifts to higher daily doses of inhaled steroids ($p < 0.001$) occurred in each group. Adherence to the self-management plans was only 65% in the PFM group and 52% in the symptoms group. Outcomes for health care utilization were similar except for fewer patients making unscheduled doctor visits within the PFM group. Our findings show that education, regular follow-up, and an action plan are effective in improving asthma control and quality of life, but the routine use of PFM to guide interventions is not the only way to accomplish these objectives.

Effects of the Prone Position on Respiratory Mechanics and Gas Exchange during Acute Lung Injury—Pelosi P, Tubiolo D, Mascheroni D, Vicardi P, Crotti S, Valenza F, Gattinoni L. Am J Respir Crit Care Med 1998;157(2):387.

We studied 16 patients with acute lung injury receiving volume-controlled ventilation to assess the relationships between gas exchange and respiratory mechanics before, during, and after 2 h in the prone position. We measured the end-expiratory lung volume (EELV, helium dilution), the total respiratory system (Cst,rs), the lung (Cst,L) and the thoracoabdominal cage (Cst,w) compliances (end-inspiratory occlusion technique and esophageal balloon), the hemodynamics, and gas exchange. In the prone position, P_{aO_2} increased from 103.2 ± 23.8 to 129.3 ± 32.9 mm Hg ($p < 0.05$) without significant changes of Cst,rs and EELV. However, Cst,w decreased from 204.8 ± 97.4 to 135.9 ± 52.5 mL/cm H_2O ($p < 0.01$) and the decrease was correlated with the oxygenation increase ($r = 0.62$, $p < 0.05$). Furthermore, the greater the baseline supine Cst,w, the greater its decrease in the prone position ($r = 0.82$, $p < 0.01$). Consequently, the oxygenation changes in the prone position were predictable from baseline supine Cst,w ($r = 0.80$, $p < 0.01$). Returning to the supine position, Cst,rs increased compared with baseline (42.3 ± 14.4 versus 38.4 ± 13.7 mL/cm H_2O; $p < 0.01$), mainly because of the lung component (57.5 ± 25.1 versus 52.4 ± 23.3 mL/cm H_2O; $p < 0.01$). Thus, (1) baseline Cst,w and its changes may play a role in determining the oxygenation response in the prone position; (2) the prone position improves Cst,rs and Cst,L when the supine position is resumed.

Time Course Evolution of Ventilatory Responses to Inspiratory Unloading in Patients—Viale JP, Duperret S, Mahul P, Delafosse B, Delpuech C, Weismann D, Annat G. Am J Respir Crit Care Med 1998;157(2): 428.

Inspiratory muscle unloading decreases ventilatory drive. In this study, we examined the time course of this effect in patients with chronic obstructive pulmonary disease receiving two modes of ventilatory support: pressure support ventilation (PSV), during which each cycle was assisted, and biphasic positive airway pressure, set up in such a manner that one spontaneous breath took place between two consecutive pressure-assisted breaths. The first breath following the switch from spontaneous breathing to PSV was associated with an increase in tidal volume (V_T) and a drop in mean transdiaphragmatic pressure (mean Pdi) and inspiratory work (WI) performed per liter but with unchanged values of esophageal occlusion pressure at 100 ms (Pes 0.1), diaphragmatic electrical activity (EMGdi), and WI performed by breath. The same phenomena were observed for the assisted breath of biphasic positive airway pressure as compared with the preceding spontaneous breath. During the subsequent breaths of PSV, Pes 0.1, EMGdi, and WI performed per breath decreased progressively up to the sixth to eighth breaths, and VT returned to pre-PSV values. We conclude that in patients with chronic obstructive pulmonary disease the decrease in ventilatory drive associated with PSV takes place from the first breath onwards but requires 6–8 breaths to be fully achieved. During biphasic positive airway pressure, as a consequence of the kinetics of the PSV-induced downregulation of ventilatory drive, assisted breaths following spontaneous breaths are characterized by an enhanced inspiratory efficiency.

Ventilator-Associated Pneumonia Caused by Potentially Drug-Resistant Bacteria—Trouillet JL, Chastre J, Vuagnat A, Joly-Guillou ML, Combaux D, Dombret MC, Gibert C. Am J Respir Crit Care Med 1998;157(2):531.

To determine risk factors for ventilator-associated pneumonia (VAP) caused by potentially drug-resistant bacteria such as methicillin-resistant *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and/or *Stenotrophomonas maltophilia*, 135 consecutive episodes of VAP observed in a single ICU over a 25-mo period were prospectively studied. For all patients, VAP was diagnosed based on results of bronchoscopic protected specimen brush (≥ 10(3) cfu/mL) and bronchoalveolar lavage (≥ 10(4) cfu/mL) specimens. Seventy-seven episodes were caused by "potentially resistant" bacteria and 58 episodes were caused by "other" organisms. According to logistic regression analysis, 3 variables among potential factors remained significant: duration of mechanical ventilation (MV) ≥ 7 d (odds ratio [OR] = 6.0), prior antibiotic use (OR = 13.5), and prior use of broad-spectrum drugs (third-generation cephalosporin, fluoroquinolone, and/or imipenem) (OR = 4.1). Distribution of the 245 causative bacteria was analyzed according to 4 groups defined by prior duration of MV (< 7 or ≥ 7 d) and prior use or lack of use (within 15 d) of antibiotics. Although 22 episodes of early-onset VAP in patients receiving no prior antibiotics were caused by antibiotic-susceptible bacteria, 84 episodes of late-onset VAP in patients receiving prior antibiotics were mainly caused by potentially resistant bacteria. Differences in the potential efficacies (ranging from 100% to 11%) against microorganisms of 15 antimicrobial regimens were studied according to classification into these 4 groups. These findings may provide a more rational basis for selecting the initial therapy of patients suspected of having VAP.

Respective and Combined Effects of Prone Position and Inhaled Nitric Oxide in Patients with Acute Respiratory Distress Syndrome—Papazian L, Bregeon F, Gaillat F, Thirion X, Gainnier M, Gregoire R, et al. Am J Respir Crit Care Med 1998;157(2):580.

Inhaled nitric oxide (NO) and prone position (PP) are two of the new therapeutics proposed in the setting of acute respiratory distress syndrome (ARDS). The aim of this study was to evaluate the hemodynamic and respiratory effects of NO and prone position in patients with ARDS. Fourteen patients, sedated, paralyzed, and ventilated using volume-control mode, were prospectively investigated. All patients had a radial artery catheter, a pulmonary artery catheter, and a 3-F fiberoptic thermistor catheter advanced via the femoral artery into the descending aorta. The protocol consisted of 7 phases: baseline measurements in supine position, SP (T0); SP + NO (T1); baseline 2 in SP (T2); PP without NO (T3); NO + PP (T4); SP + NO (T5); and PP + NO (T6). Inhaled NO (T1) induced an increase in PO_2/F_{IO_2} (from 128 ± 44 to 180 ± 75 mm Hg, $p < 0.004$). Prone position (T3) resulted in an increase in PO_2/F_{IO_2} (193 ± 83 mm Hg, $p < 0.003$ versus T0). The association of NO with PP (T4) resulted in a significant improvement in PO_2/F_{IO_2} (261 ± 98 mm Hg) when compared with T0, T1, and T3. Analysis of variance showed a significant and additive effect of NO and PP on both PO_2/F_{IO_2} ($p < 0.000$) and shunt fraction (QS/QT) ($p < 0.01$). Since the association of NO with PP presents additive effects on oxygenation, this association can be proposed for the treatment of ARDS.

Self-Control and External Control of Mechanical Ventilation Give Equal Air Hunger Relief—Bloch-Salisbury E, Spengler CM, Brown R, Banzett RB. Am J Respir Crit Care Med 1998;157(2):415.

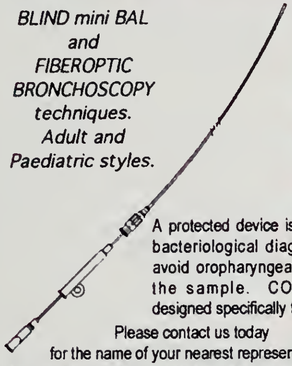
Elevated end-tidal partial pressure of CO_2 ($PETCO_2$) causes air hunger; this sensation becomes intense with a relatively small rise in $PETCO_2$ if ventilation is held constant. Spontaneously breathing subjects increase ventilation in response to CO_2, thereby greatly diminishing air hunger. In healthy subjects and ventilator-dependent patients, experimenter-induced increases in ventilator tidal volume (V_T) relieve air hunger even if $PETCO_2$ is kept elevated. We addressed two questions: (1) Can paralyzed, ventilator-dependent patients use the sensation of air hunger to effectively control ventilator V_T using nonrespiratory motor pathways; and (2) Do subjects obtain more relief when in control of their own ventilator? Four subjects were trained to increase ventilator V_T using a mouth-operated switch. Subjects' ratings of air hunger intensity in response to elevated $PETCO_2$ were compared during 3 conditions: (1) constant V_T; (2) subject-controlled V_T; and (3) experimenter-controlled V_T. When given control of their ventilator, all subjects increased V_T in response to increased $PETCO_2$, thereby relieving air hunger. Air hunger relief was similar when the experimenter mimicked these V_T changes. These results suggest that: (1) ventilator-dependent patients can use sensation, conscious decisions, and nonrespiratory motor pathways to achieve an appropriate respiratory response to increased P_{CO_2} and (2) control of one's own ventilation is unimportant in these circumstances.

Effect of Lung Volume Reduction Surgery on Neuromechanical Coupling of the Diaphragm—Laghi F, Jubran A, Topeli A, Fahey PJ, Garrity ER Jr, Arcidi JM, et al. Am J Respir Crit Care Med 1998;157(2):475.

The mechanisms for symptomatic improvement following lung volume reduction surgery for emphysema are poorly understood. We hypothesized that enhanced neuromechanical coupling of the diaphragm is an important factor in this improvement. We studied 7 patients with diffuse emphysema before and 3 mo after surgery. Patients showed improvements in 6-min walking distance ($p = 0.002$) and dyspnea ($p = 0.04$). The pressure output of the respiratory muscles, quantified as pressure-time product per minute (PTP/min), decreased after surgery ($p = 0.03$), as did P_{aCO_2} ($p = 0.02$). Maximal transdiaphragmatic pressures (P_{dimax}) increased from 80.3 ± 9.5 (SE) to 110.8 ± 9.3 cm H_2O after surgery ($p = 0.03$), and the twitch transdiaphragmatic pressure response to phrenic nerve stimulation (P_{ditw}) increased from 17.2 ± 2.4 to 25.9 ± 3.0 cm H_2O ($p = 0.02$); these increases were greater than could be accounted for by a decrease in lung volume. The contribution of the diaphragm to tidal breathing, assessed by relative changes in gastric and transdiaphragmatic pressures, increased after surgery ($p = 0.008$). Net diaphragmatic neuromechanical coupling, quantified as the quotient of tidal volume (normalized to total lung capacity) to tidal change in Pdi (normalized to P_{dimax}), improved after surgery ($p = 0.03$) and was related to the increase in 6-min walking distance ($r = 0.86$, $p = 0.03$) and decrease in dyspnea ($r = 0.76$, $p = 0.08$). In conclusion, lung volume reduction surgery effects an improvement in diaphragmatic function, greater than can be accounted for by a decrease in operating lung volume, and enhances diaphragmatic neuromechanical coupling.

Variations in the NRAMP1 Gene and Susceptibility to Tuberculosis in West Africans—Bellamy R, Ruwende C, Corrah T, McAdam KP, Whittle HC, Hill AV. N Engl J Med 1998;338(10):640.

BACKGROUND: Genetic factors may affect the susceptibility to tuberculosis, but no specific genes governing susceptibility have been identified. In mice, natural resistance to infection with some mycobacteria is influenced by the gene for natural-resistance-associated macrophage protein 1 (Nramp1), but the role of the human homologue of this gene, NRAMP1, in tuberculosis is unknown. We typed polymorphisms in NRAMP1 in a case-control study of tuberculosis in the Gambia, West Africa. METHODS: Sequence-specific oligonucleotide hybridization and microsatellite analysis were used to type NRAMP1 polymorphisms in 410 adults (mean age, 34.7 years) with smear-positive pulmonary tuberculosis and 417 ethnically matched, healthy controls. Patients with human immunodeficiency virus infection were excluded. RESULTS: Four NRAMP1 polymorphisms were each significantly associated with tuberculosis. Subjects who were heterozygous for two NRAMP1 polymorphisms in intron 4 and the 3' untranslated region of the gene were particularly overrepresented among those with tuberculosis, as compared with those with the most common NRAMP1 genotype (odds ratio, 4.07; 95 percent confidence interval, 1.86 to 9.12; chi-square = 14.58; $p < 0.001$). CONCLUSIONS: Genetic variation in NRAMP1 affects susceptibility to tuberculosis in West Africans. *See the related editorial:* **The Evolving Relation between Humans and Mycobacte-**



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rium Tuberculosis. Bloom BR, Small PM. N Engl J Med 1998;338(10):677–678.

An Outbreak Involving Extensive Transmission of a Virulent Strain of Mycobacterium Tuberculosis—Valway SE, Sanchez MP, Shinnick TF, Orme I, Agerton T, Hoy D, et al. N Engl J Med 1998;338(10):633.

BACKGROUND & METHODS: From 1994 to 1996, there was a large outbreak of tuberculosis in a small, rural community with a population at low risk for tuberculosis. Twenty-one patients with tuberculosis (15 with positive cultures) were identified; the DNA fingerprints of the 13 isolates available for testing were identical. To determine the extent of transmission, we investigated both the close and casual contacts of the patients. Using a mouse model, we also studied the virulence of the strain of Mycobacterium tuberculosis that caused the outbreak. RESULTS: The index patient, in whom tuberculosis was diagnosed in 1995; the source patient, in whom the disease was diagnosed in 1994; and a patient in whom the disease was diagnosed in 1996 infected the other 18 persons. In 5, active disease developed after only brief, casual exposure. There was extensive transmission from the 3 patients to both close and casual contacts. Of the 429 contacts, 311 (72%) had positive skin tests, including 86 with documented skin-test conversions. Mice infected with the virulent Erdman strain of *M. tuberculosis* had approximately 1000 bacilli per lung after 10 days and about 10,000 bacilli per lung after 20 days. In contrast, mice infected with the strain involved in the outbreak had about 10,000 bacilli per lung after 10 days and about 10 million bacilli per lung after 20 days. CONCLUSIONS: In this outbreak of tuberculosis, the growth characteristics of the strain involved greatly exceeded those of other clinical isolates of *M. tuberculosis*. The extensive transmission of tuberculosis may have been due to the increased virulence of the strain rather than to environmental factors or patient characteristics. *See the related editorial:* **The Evolving Relation between Humans and Mycobacterium Tuberculosis.** Bloom BR, Small PM. N Engl J Med 1998;338(10):677–678.

Deaths from Unintentional Carbon Monoxide Poisoning and Potential for Prevention with Carbon Monoxide Detectors—Yoon SS, Macdonald SC, Parrish RG. JAMA 1998; 279(9):685.

CONTEXT: Unintentional carbon monoxide (CO) poisoning causes approximately 2100 deaths in the United States per year, but the use of CO detectors could potentially prevent many of these deaths. OBJECTIVE: To describe the epidemiology of potentially preventable unintentional CO poisoning deaths in New Mexico. DESIGN: Descriptive analysis. POPULATION STUDIED: A total of 136 deaths from CO poisoning investigated by the New Mexico Office of the Medical Investigator, 1980 through 1995. MAIN OUTCOME MEASURES: Characteristics of deaths from CO poisoning; estimates of the number of deaths potentially preventable with CO detectors. RESULTS: Of 136 people whose deaths were classified as "unintentional carbon monoxide poisoning, not fire related," 49 (36%) most likely were asleep when poisoned. Thirty-nine (49%) of 80 people whose deaths were identified as "residential fatalities" most likely were asleep vs 10 (18%) of 56 of those whose deaths were identified as occurring in or around motor vehicles. A blood-alcohol level greater than 0.01% was present in 56 (42%) of the decedents. Among decedents who had a negative blood-alcohol level (52 in residences and 26 in vehicles), an electronic audible CO detector may have prevented CO poisoning; whereas, among those who had a negative blood-alcohol level and most likely were awake at the time of CO exposure (28 in residences and 23 in vehicles), an electronic detector or a nonaudible, chemical reagent type detector may have prevented CO poisoning. CONCLUSION: Differences exist between deaths due to unintentional CO poisoning that occur in residences and those that occur in or around motor vehicles. Carbon monoxide detectors, whether the electronic or chemical reagent types, may have prevented approximately half of these deaths. The high proportion of decedents with alcohol in their blood indicates that effective public health campaigns must address the role of alcohol in CO poisoning deaths.

Effect of Pneumonia and Whooping Cough in Childhood on Adult Lung Function—Johnston ID, Strachan DP, Anderson HR. N Engl J Med 1998;338(9):581.

BACKGROUND: Previous studies have suggested that respiratory infection during childhood is associated with respiratory disease in adulthood, but the link is unclear because of retrospective ascertainment of childhood infection, selection bias, and confounding factors. METHODS: We studied the effects of childhood pneumonia and whooping cough in 1,392 British adults followed from birth in 1958. Of these, 193 had a history of pneumonia and 215 a history of whooping cough by the age of 7 years. When the subjects were 34 or 35 years old, their forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were measured before and after they inhaled albuterol. RESULTS: A history of pneumonia was associated with deficits (± 95% confidence limits) in both FEV_1 (102 ± 73 mL, p = 0.006) and FVC (173 ± 70 mL, p = 0.001) when the analysis was adjusted for sex, height, and smoking, with no change in the ratio of FEV_1 to FVC. These deficits persisted after inhalation of albuterol. In subjects with no history of wheezing, the deficit in FEV_1 was 155 ± 122 mL (p = 0.01), in those with past wheezing it was 41 ± 128 mL (p = 0.53), and in those with current wheezing it was 119 ± 133 mL (p = 0.08). The effect was no greater for the subjects who had pneumonia at less than two y of age than for those who had it between the ages of 2 and 7 years and was not diminished after control for multiple confounding factors. The deficits associated with whooping cough were smaller (FEV_1, 41 ± 70 mL; p = 0.25; FVC, 81 ± 76 mL; p = 0.04). CONCLUSIONS: Childhood pneumonia is associated with reduced ventilatory function in adults. This reduction is independent of a history of wheezing and is not explained by other confounding factors.

Delivery of Hyperbaric Oxygen Therapy to Critically Ill, Mechanically Ventilated Children—Keenan HT, Bratton SL, Norkool DM, Brogan TV, Hampson NB. J Crit Care 1998; 13(1):7.

PURPOSE: The purpose of this article is (1) to describe our method of mechanical ventilation and monitoring of critically ill children during administration of hyperbaric oxygen therapy (HBO_2) in a multiplace chamber; and (2) to review the complications they experienced during transport to the HBO_2 chamber and HBO_2 treatment. MATERIALS & METHODS: A case series from a university-affiliated children's hospital and regional hyperbaric medicine treatment facility. Patients studied included all children who required HBO_2 therapy while mechanically ventilated at any time between April 1985 and June 1995. RESULTS: Thirty-two children were treated with HBO_2 while mechanically ventilated. Ages ranged from 3 days to 11.3 years (mean 4.8 ± 3.5 years). There were 22 males. Twenty-one children had necrotizing infections, 9 had carbon monoxide (CO) poisoning, and 2 had iatrogenic arterial air embolism. Complications or events occurring during HBO_2 therapy included hypotension (63%), bronchospasm (34%), hemotympanum (13%), and progressive hypoxemia (6%). The only complication during transport was one accidental extubation (3%). CONCLUSION: Hyperbaric oxygen therapy can be administered safely to most critically ill children in a multiplace chamber if they are monitored closely. Although complications are not uncommon, most can be managed easily by a team skilled in treating ill children and knowledgeable of possible complications of HBO_2 therapy.

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Aerosol Therapy with Metered Dose Inhalers during Mechanical Ventilation: The Need for In Vitro Tests

The manufacturers of metered dose inhalers (MDIs) provide a high-quality product. The purity, stability, and potency of the drug in the MDI formulation are ensured, and the "shot potency" of MDIs is tested for accuracy and reproducibility for the specified number of doses.[1] The mass median aerodynamic diameter (MMAD) and geometric standard deviation of the aerosol particles are measured by use of a variety of multistage impactors.[2,3] Aerosol particle size is also determined by use of light-scattering devices, single-particle optical sizers, aerodynamic particle sizers, or automatic image analyzers with optical microscopes.[3] The primary purpose of such tests is to determine the fraction of the dose contained within fine, respirable particles, eg, those $< 5\ \mu m$ in aerodynamic diameter.[4,5] Theoretically, these particles should deposit in the lungs.[4] In addition, there is a large body of literature proving the efficacy of these devices in clinical use.[6] For these reasons, further in vitro testing of MDIs may be of questionable value.

See The Original Study on Page 705

Although the current standards of in vitro testing are vital for ensuring quality control of aerosols generated by MDIs, their clinical application is limited. Various laboratory tests cannot accurately predict the fraction of an MDI dose that will deposit in the patient's lower respiratory tract. The "respirable mass" and the "fine particle fraction" have been suggested as predictors of aerosol deposition within the lung;[2,4,5] however, the clinical relevance of these measurements has not been established.[7] A more precise laboratory model could provide reference standards that would be of immense value in making the results obtained from in vitro tests more meaningful for clinicians.

There are several reasons for the lack of correlation between aerosol deposition predicted by in vitro tests and the values measured in vivo. First, in vitro testing with a cascade impactor, the reference standard for testing MDIs, uses a constant air flow. In contrast, tidal volume, inspiratory air flow, breathing frequency, and mouth versus nose breathing vary widely among patients. The performance of MDIs under these diverse conditions cannot be tested with a cascade impactor. Moreover, cascade impactors do not reliably measure the effect of actuation that is asynchronous with inspiration, a common problem among patients using MDIs.[8,9] Variations in the anatomy of the upper airway among individuals, particularly in the size of the larynx, make it extremely difficult to correlate data obtained in vitro by use of cascade impaction with actual in vivo lung deposition.[10] Therefore, additional in vitro tests are needed to determine the efficiency of aerosol-generating devices under a variety of conditions encountered in clinical practice.

Second, the need for in vitro testing arises when an MDI is combined with an accessory device. For example, when a spacer is used with an MDI, many factors influence drug output: dimensions and shape of the spacer; material used to manufacture the spacer; number, position, design, and size of the baffles; electrostatic charge on the inner surface of the device; number of doses actuated into the device per inhalation; and the interval between actuation and inhalation.[11–15] Clark and Lipworth[14] found a 2-fold reduction in the systemic bioavailability of albuterol in healthy volunteers who delayed inspiration from a spacer and when multiple puffs were discharged into the spacer before inhalation. Therefore, the performance of an MDI in combination with an accessory device can differ significantly from that of the MDI alone.

Finally, the use of aerosol-generating devices in diverse clinical situations requires testing with in vitro models that simulate the specific clinical scenario, such as aerosol therapy in infants and children and for patients with different diseases. Moreover, a multitude of factors influence aerosol therapy during mechanical ventilation, [16] and many of these factors differ from those that influence aerosol therapy in ambulatory, nonintubated patients. For example, millions of ambulatory patients use MDIs on a daily basis, but an MDI cannot be used in a ventilator circuit with the actuator supplied by the manufacturer. Once the canister is uncoupled from its original actuator, it and the new actuator become a unique device with aerosol characteristics and performance that differ from those of the original canister-actuator combination. In addition, the breathing pattern of mechanically ventilated patients is different from

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that of nonintubated patients. Thus, laboratory tests can help verify the performance and efficiency of various MDI devices during mechanical ventilation.

Several investigators have successfully modeled the patient-ventilator interface in vitro.[17–24] These investigations found that aerosol delivery depends on the type of spacer, humidity in the ventilator circuit, synchronization of aerosol actuation with inspiratory air flow, and the ventilatory parameters used during mechanical ventilation.

In an important investigation reported in this issue of Respiratory Care, [25] Rau et al compare the efficacy of 5 different spacer devices in a model of mechanical ventilation: a novel, bidirectional, inline spacer, the Airlife MiniSpacer (Allegiance Healthcare Corp, McGaw Park, IL), another inline spacer (Hudson RCI®, Temecula CA), and 3 chamber spacers (AeroVent, Monaghan Medical Corp, Plattsburgh, NY; Aerosol Cloud Enhancer [ACE], DHD Healthcare, Canastota NY; and Airlife MediSpacer, Allegiance Healthcare Corp). Rau et al found differences of 3- to 4-fold in drug delivery beyond the endotracheal tube among the various devices tested. The bidirectional inline spacer performed as efficiently as some spacer chambers, and was superior to the unidirectional inline spacer. Moreover, the performance of the various devices varied with the type of MDI (albuterol/flunisolide) used. This investigation is probably the first to report differences in the delivery of flunisolide with various spacers. Thus, all the spacers delivered lesser amounts of flunisolide (as a percent of the nominal dose) than albuterol (range 30–59% decrease in flunisolide vs albuterol delivery). Although inhaled corticosteroids are not commonly administered to mechanically ventilated patients,[26,27] the decrease in flunisolide output is applicable to its use with other accessory devices in nonintubated patients. Such discrepancies in drug delivery are likely to translate into differences in therapeutic response when flunisolide is administered by use of various accessory devices.

Spacer devices that are used to connect MDIs in ventilator circuits include elbow adapters, inline devices, and chamber or reservoir adapters. The elbow adapters connect to the endotracheal tube, whereas the inline and chamber adapters are placed in the inspiratory limb of the ventilator circuit.[28] The jet produced by an MDI exits the actuator at the speed of a car on an interstate expressway, rapidly expands into a flume, and dissipates within 100 msec in still air.[29] This information is pertinent to aerosol therapy with MDIs during mechanical ventilation. Actuation of the aerosol device at a distance from the endotracheal tube allows the velocity of the jet to decrease before encountering the narrowest part of the ventilator circuit and reduces losses due to inertial impaction. Moreover, the use of a chamber spacer allows the flume to expand without impacting on the walls of the device. Propellant evaporation in the expanding flume decreases the size of the drug particles before entrainment in the inspiratory air flow. The ventilator circuit acts as an extended baffle, and only fine particles (diameter ≤ 2 μm)[23] can successfully negotiate the many impediments in their path en route to the distal end of the endotracheal tube.

The finding by Rau et al that the chamber spacers performed better than the unidirectional inline spacer agrees with those of previous investigators.[20,23] However, the use of a bidirectional inline spacer is a novel concept. Such a spacer increases the volume of air into which the aerosol is actuated and correspondingly produces a 1.5- to 2.5-fold increase in aerosol delivery compared with that achieved with the unidirectional inline spacer. Of interest, the dimensions of the bidirectional spacer were much smaller than those of the chamber spacers, but its efficiency of drug delivery was comparable with that of 2 (AeroVent and ACE) of the 3 chamber spacers.

The investigation of Rau et al has several merits. They used a humidified ventilator circuit to better simulate the conditions encountered in clinical practice. Humidified ventilator circuits reduce aerosol delivery by 40–50% compared with delivery using dry circuits.[17,18,23,24] Previous in vitro investigations were done using dry ventilator circuits; however, mechanically ventilated patients receive warmed and humidified gases. Thus, humidity in the ventilator circuit was a major reason for the discrepancy between in vitro and in vivo values of aerosol delivery during mechanical ventilation.*[16] The ventilator settings used by Rau et al correspond to the ventilatory parameters commonly used in patients. Moreover, they directly measured drug deposition on filters to quantitate aerosol delivery, and the location of the devices in the ventilator circuit was appropriate and clinically feasible. The distance from the endotracheal tube was not comparable for all of the devices. However, this difference is unlikely to have contributed significantly to the variations in drug output among the various devices.

One limitation of the study by Rau et al is that MDI actuation was not synchronized with inspiration for all of the devices. While actuation was synchronized with inspiration when the inline spacers and MediSpacer were used, there was a 1-s delay between actuation and inspiration with the AeroVent and ACE. Diot et al[23] showed that a 1-s to 1.5-s delay decreases the efficiency of the AeroVent by 35%. A similar effect could occur with the ACE. Thus, a 1-s delay between actuation and inspiration may have contributed to the observed differences in aerosol delivery by the AeroVent or ACE spacer versus the MediSpacer. Despite this drawback, Rau et al are correct in concluding that the outcome of therapy may be influenced by the efficiency of the device used to actuate the MDI in the ventilator circuit. The impact of the spacer on aerosol delivery was pointed out by Newhouse and Fuller in a classic editorial.[30] Subsequently, a few clinical trials have confirmed that the response to bronchodilator therapy administered with an MDI in mechanically ventilated patients depends on the type of spacer used to actuate the MDI in the ventilator circuit.[31–33]

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*James B Fink, Hines VA Hospital, Hines IL, 1998: personal communication.

Rau and colleagues raise another important issue, ie, the difference in the performance of various spacers with different drug canisters. The use of flunisolide instead of albuterol reduced the dose of the drug emitted from various spacers by 30–59%. Ahrens and colleagues[34] reported that the performance of 4 chamber devices in combination with 4 different MDI canisters differed not only between spacer devices, but the performance of each device varied with the type of MDI canister used. Similarly, albuterol formulations containing chlorofluorocarbon versus hydrofluoroalkane propellants in combination with various spacers[*35] and albuterol versus salmeterol canisters used with the AeroVent, ACE, and MediSpacer in a model of mechanical ventilation show differences in drug output (personal observation). Thus, each spacer and drug canister combination is unique, and a universal actuator or adapter that can work equally well with a variety of drug canisters has not been developed. In addition to the differences in the diameter and design of the canister nozzle, the pressure inside the canister, the concentration of the drug, the size of the orifice in the actuator or adapter, and the ambient temperature influence the amount and characteristics of the aerosol generated by an MDI-spacer combination.[15] Therefore, in vitro tests are necessary to verify the efficiency of any canister when used in combination with an actuator other than that designed by the manufacturer.

A product with all the desirable characteristics of a good aerosol-generating device may perform well in certain clinical situations but not in others. In vitro tests ensure that various devices perform efficiently in appropriately simulated clinical situations. Successful aerosol therapy in mechanically ventilated patients requires meticulous attention to the technique of administration. In vitro tests have identified subtle differences in the use of MDIs that influence the fraction of the aerosol delivered to the lower respiratory tract of mechanically ventilated patients. Carefully performed in vitro tests can be of great value in guiding aerosol therapy during mechanical ventilation.

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Respiratory Care Protocols: How Can the 'Time Required For Change' Be So Protracted?

As I get older, I become more impatient with health care options that seem to have inordinately long gestation periods. This very week, for example, has been spent in frustrating dialog with the Health Care Financing Administration regarding the role and function of respiratory care practitioners (RCPs) in skilled nursing facilities (SNFs). As the Prospective Payment System (PPS) is rolled out, it appears that RCPs will be replaced in many of the facilities by variously trained, skilled and credentialled members of the nursing service, whose qualifications to deliver respiratory care services are questionable, at best.[1]

I have the uncomfortable feeling that I (we) have been down this road before! Indeed, review of my own experience reveals that we have had these *very same* conversations with reimbursement agencies before—in 1970, for example, in a similar furor with Blue Cross/Blue Shield in California! Misallocation of respiratory care revenues was the issue then, although it was referred to in those halcyon days as 'appropriateness.' Then, and now, it was (is) 'time for a change' in which RCPs need to step up to the plate and *prove* that their assessment, treatment selection, and technical delivery skills characterize *them* as the best trained, most competent allied health care workers to deliver these services. therapist-driven protocols (TDPs) have allowed the profession a venue for these demonstrations.

In an article which appears in this volume of Respiratory Care,[2] the author, Dr James Stoller, does not refer to one of his own publications,[3] which five years ago suggested that the 'time for a change' might well be upon us. Then, and now, he pointed out the need for additional studies to evaluate the soundness of the respiratory care protocol/therapist driven protocol paradigm. Indeed! In the era of evidence-based medicine, one can hardly argue with his desire for more prospective, randomized controlled trials of both the clinical and financial aspects of the TDP approach, or for better mechanisms by which the TDP paradigm can be used more effectively in the training of house-staff physicians, and for that matter, respiratory care students.

I would suggest that the reader consider Stoller's review[2] in light of the current PPS conundrum. In SNFs, home health agencies and other 'nontraditional' sites remote to hands-on medical direction and direct physician involvement, the TDP 'movement' has gained a measure of acceptance as a cost-effective paradigm to enhance appropriate allocation of respiratory care services. In SNFs, for example, physicians are required to make rounds (at a minimum) only once in 30 days. Registered nurses, whose standards[4] suggest that *they* are competent to perform such services, need to be present only 40 hours per week; the clear majority of residents (patients) cannot be expected to give respiratory treatments to themselves! And yet, despite all sorts of appeals to logic, RCPs are in great danger of being *regulated out* of SNF work by the PPS.

What a great opportunity for appropriately controlled studies of outcomes to serve as grist for Dr. Stoller's mill! I believe that such studies (in SNFs) will identify an enormous amount of *under*-utilization, compared to the rank over-utilization seen in the acute care setting. RCPs working in SNFs will need to understand that the need for their services may not be apparent on the admission MDS-II (Minimum Data Set) form. Indeed, things regularly "go bump in the night" in such facilities, often with less than classic clinical presentations: acute bronchospasm, aspiration of gastric contents, nosocomial pneumonia, tuberculosis, pulmonary embolism, congestive heart failure, atelectasis, and acute respiratory failure constitute my 'short list' of such conditions.

It is becoming clear that cost savings alone are but a portion of the TDP windfall. Clinical outcomes and uniformity of care through consistent adherence to data-based, rational standard clinical practice guidelines appear to be enhanced, in addition to modest conservation of financial resources.

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The RCP who knows answers to the questions, "What's going on here?" "How severe is the problem?" and "What can be done about it?" is truly *protocol safe and ready*. The immediate future will test his or her competitive edge in the PPS-driven SNF beyond the July 1, 1998 imple-

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mentation date. The respiratory care profession's own internal documents suggest that he or she has been taught[5] and tested[6] more thoroughly than other health professionals clustered around the respiratory patient's bedside.

From now on *competence* will be the real issue. The time for a change has arrived!

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A Comparison of Inline MDI Actuators for Delivery of a Beta Agonist and a Corticosteroid with a Mechanically Ventilated Lung Model

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INTRODUCTION: The type of metered dose inhaler (MDI) actuator/adaptor as well as the type of drug used may influence the dose of drug delivered to intubated, ventilated subjects. PURPOSE: **The purpose of this study was to evaluate MDI aerosol drug delivery of albuterol (Proventil®) and flunisolide (AeroBid®) through an endotracheal tube (ETT) using a novel bidirectional nonreservoir actuator , the Allegiance Healthcare Corp Airlife MiniSpacer (MiniSpacer) in comparison with four other MDI actuator/reservoir devices. METHODS: The MiniSpacer was compared to the DHD Healthcare Aerosol Cloud Enhancer (ACE), the Allegiance Healthcare Corp Airlife MediSpacer (MediSpacer), the Monaghan Medical Corp AeroVent (AeroVent), and the Hudson RCI® Inline MDI Adaptor (Hudson Inline) for MDI administration of albuterol and flunisolide, using a mechanically ventilated lung model. Drug dose was collected at the end of the ETT on a filter and was analyzed by spectrophotometer. Drug delivery at the end of the ETT is expressed as a percent of the dose measured from the MDI. RESULTS: Mean (standard deviation) doses of albuterol were: Hudson Inline—12.0% (0.9), MiniSpacer—17.2% (1.2), AeroVent—17.7% (2.5), ACE—30.0% (2.0), and MediSpacer—31.8% (1.6). Mean (standard deviation) doses of flunisolide were: Hudson Inline—5.0% (0.9), AeroVent—11.4% (1.8), ACE—12.4% (2.8), MiniSpacer—13.1% (2.2) and MediSpacer—21.0% (1.8). There were significant differences across device types ($p < 0.005$), for both albuterol and flunisolide delivery by one-way analysis of variance (ANOVA). CONCLUSION:** **The new nonreservoir bidirectional MDI adaptor (MiniSpacer) was superior to the unidirectional Hudson nonreservoir adaptor in dose delivery through an ETT for both albuterol and flunisolide. For delivery of albuterol, the bidirectional adaptor was equivalent to the AeroVent reservoir but not as efficient as the MediSpacer or ACE reservoirs. For delivery of flunisolide, the bidirectional adaptor was equivalent to both the ACE and the AeroVent, but lower than the MediSpacer. Delivery of the corticosteroid flunisolide was lower for all devices compared to albuterol.** [Respir Care 1998;43(9):705–712] *Key words: Aerosol delivery, inline MDI activators, lung models, mechanical ventilation, metered dose inhalers, spacer devices.*

Introduction

There are a variety of devices available for administering metered dose inhaler (MDI) medications to intubated patients on mechanical ventilation. Previous in vitro and in vivo testing has shown that the type of MDI actuator can influence the dose of drug delivered at the end of the endotracheal tube (ETT). Elbow actuator/adaptors on the ETT were generally found to deliver less bronchodilator drug through an ETT when compared to reservoir devices.[1–3] An in vitro study by Bishop et al found that a T-type actuator (Instrumentation Industries RTC-22) placed inline proximal to the

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Dr Rau presented a version of this paper during the annual OPEN FORUM at the 43rd International Respiratory Congress, December 6–9, 1997, in New Orleans, Louisiana.

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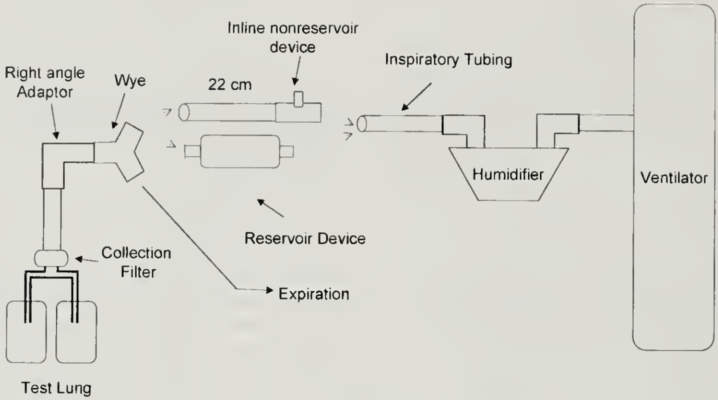

Fig. 1. Equipment configuration for in vitro lung model testing of reservoir and nonreservoir MDI actuating devices for inline ventilator delivery.

patient Y, delivered a greater volume of aerosol bronchodilator drug particles in the 1–5 μm size range than the elbow type of adaptor, but less volume compared to a reservoir device (the Monaghan AeroChamber inline spacer*).[1] The in vivo study by Fuller et al reported that an inline T-type device delivered less bronchodilator drug to the lungs than either reservoir devices of varying volume or an elbow type of adaptor.[3] The T-type adaptor is often referred to as an inline nonchamber, or nonreservoir, device. The nonreservoir inline MDI adaptors have minimal volume compared to reservoir devices, and this may account for the lower drug delivery with the T-type devices.[3-4] The type of MDI drug used, such as β_2 agonist or corticosteroid, has also been shown by Ahrens et al to affect the delivery performance of reservoir devices.[5] This variation may affect performance of nonreservoir inline T-type adaptors as well, and has not been evaluated in the literature.

Recently a novel inline, nonreservoir type of MDI actuator has been developed by Thayer Medical Inc, and marketed by Allegiance Healthcare Inc, which offers a bidirectional aerosol spray when placed inline in the inspiratory limb of a ventilator breathing circuit. This design theoretically offers a greater holding volume for the aerosol, compared to the unidirectional spray from previous inline nonreservoir actuators. The increased volume for the aerosol spray plume may improve drug delivery for this type of nonreservoir device. The purpose of this study was to evaluate dose delivery of an MDI bronchodilator and corticosteroid drug through an ETT with the nonreservoir bidirectional adaptor compared to 3 available reservoir devices and a unidirectional inline nonreservoir device, using a mechanically-ventilated adult lung model.

Materials and Methods

Lung Model A Puritan Bennett Model MA-1 (MA-1) provided positive pressure breaths to a dual-chambered test lung, with Compliance setting = 50 mL/cm H_2O, and Resistance set by the 8.0 mm tubing of the test lung, using a disposable adult ventilator circuit (Dart Respiratory, Uni-Set). The MA-1 volume setting was adjusted to achieve a delivered volume of approximately 800 mL to the test lung at a respiratory rate = 10/min and flow = 60 L/min. Use of the lung simulator provided both an inspiratory and expiratory phase during drug dose measures. Volume, inspiratory flow, and respiratory rate were verified prior to dose measure, using the BioTek adult ventilator testor, Model VT-1. The test lung and the expiratory limb of the ventilator circuit were isolated using a high efficiency particulate air (HEPA) filter to prevent aerosol drug contamination of the lung or environment. A servo-controlled Fisher & Paykel heated humidifier (Model MR 480) was used to provide approximate saturation of inspired gas between 30–35° C, as measured at the circuit Y-piece. A right angle adaptor connected the circuit Y-piece to an 8.0 mm inner diameter ETT. Aerosol drug was collected on a filter between the end of the ETT and the test lung. The distal tip of the ETT was inserted through a 15 mm adaptor and the cuff inflated. The adaptor was inserted into the larger 22 mm port of the collecting filter, with the Murphy eye and tip projecting into the filter housing but not touch-

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*Suppliers of commercial products are identified in the Product Sources section at the end of the text.

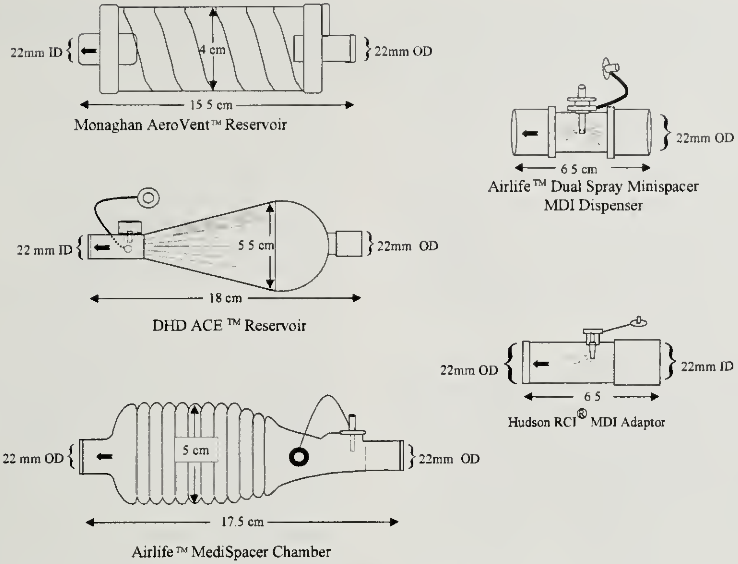

Fig. 2. Diagram of reservoir and nonreservoir MDI actuating devices for inline ventilator delivery, giving dimensions of each device and direction of aerosol drug spray. Device illustrations are not to scale with respect to each other.

ing the filter material. A diagram of the configuration is shown in Figure 1. The ETT was oriented horizontally to prevent condensation and wash-through of aerosol drug to the collecting filter, and the natural curve of the ETT was preserved during dose delivery. The predictive validity of in vitro bench tests of aerosol delivery has been established by Fuller et al and by O'Riordan et al.[6–7] In their studies, in vitro results generally gave higher absolute amounts of drug delivery compared to in vivo, but proportional differences between devices or delivery methods remain accurate.

The bidirectional actuator/adaptor T (MiniSpacer) was compared with four other brands of MDI actuator/adaptor: the DHD Healthcare Inc Aerosol Cloud Enhancer (ACE), the Allegiance Healthcare Corp Airlife MediSpacer (MediSpacer), the Monaghan Medical Corp AeroVent (AeroVent), and the Hudson RCI® Inline MDI Adaptor (Hudson Inline). Diagrams of the five MDI adaptors are shown in Figure 2. Assembly of reservoirs and actuator/adaptors followed manufacturers' specifications. The ACE, AeroVent and MediSpacer reservoirs were placed on the inspiratory limb of the ventilator circuit, just proximal to the Y-piece. The ACE was placed in a reverse-firing position, and the MediSpacer and AeroVent reservoirs in a forward-firing position. Both the Hudson Inline adaptor and the MiniSpacer were placed in the inspiratory limb of the ventilator circuit, 22 cm upstream from the Y-piece, to allow comparison with the in vivo study of an inline nonreservoir device as reported in Fuller et al.[3]

Study Design Using a separate MDI of the drug being tested, 5 actuations of albuterol (Proventil®) or of flunisolide (AeroBid®), respectively, were discharged initially through each device to be tested, and then the reservoir/adaptor washed and dried prior to any test dose measures. This was intended to remove or lessen any electrostatic charge which may affect the dose delivery measures on new and unused devices.[8–9]

The same MDI canister and ETT were used for dose measurement for each sample set of the 5 different brands of MDI actuating devices, to minimize dose variability due to different MDIs or tubes. Between each dose measurement with a brand in a sample set, the ETT and connectors were rinsed with distilled water and dried. A new MDI canister and ETT were assigned to each set of 5 brands. A total of 6 different MDIs were used for each drug tested, one for each sample set of 5 brands of actuating device. No MDI canister used for dose measures exceeded 50% exhaustion, to further ensure accurate doses. Full MDI canisters were obtained for the trials and weighed to verify equivalent fullness. Each new canister had 5 actuations discharged prior to its first use for dose measures. Canisters were shaken prior to use; one actuation was discharged to prime the valve if the canister had not been used in the preceding 4 hours. The ventilator circuit and each MDI actuator device were allowed to warm up and stabilize at the desired temperature range of 30–35° C.

The dose from each of the 6 MDIs used for testing was measured separately. The mouthpiece/actuator of the MDI was attached directly to the collecting filter, which was connected to a vacuum pump operated at a constant 30 L/min. For albuterol, a total of 5 actuations were delivered to the filter, with 30-second intervals and shaking between actuations. The MDI dose of flunisolide was similarly measured, using 3 actuations.

For measurement of albuterol delivery through the ETT, 12 MDI actuations were used to provide an adequate amount of drug on the filter for accurate dose measurement. The nominal dose of albuterol with each actuation is 100 μg from the canister valve. Similarly, for testing of flunisolide delivery, 5 MDI actuations were used to provide adequate drug on the filter for measurement. The nominal dose of flunisolide is 250 μg from the valve per MDI actuation. Drug amounts collected at the end of the ETT were then expressed as dose per actuation, as a percent of the previously measured MDI dose. The order was rotated in which each of the 5 brands was tested. Six samples of each of the 5 brands were tested, with both albuterol and flunisolide. Separate sets of the 6 samples were used for the 2 different drugs tested.

All MDI actuations with the actuators tested were synchronized with the beginning of inspiration, following the manufacturers' instructions. For the MediSpacer and the inline nonreservoir MiniSpacer, MDI actuation coincided with a manually triggered inspiration, using a simple count rhythm. For the ACE and AeroVent, MDI actuation preceded a manually triggered inspiration by approximately 1 second, using the same count rhythm. Since no instructions were given with the Hudson actuator for the timing of MDI actuation and inspiration, the MDI actuation coincided with the manually triggered inspiration as with the MediSpacer and MiniSpacer. Following each MDI actuation, the ventilator delivered 4 more breaths at the rate of 10/min, to give a total of 30 seconds between each MDI actuation for valve refill. The MDI was shaken between each of the individual actuations. Actuation intervals of 30 seconds, with shaking between actuations, did not affect MDI total or respirable dose (defined as < 6.8 μm) in Everard et al's study.[10] The same operator activated all MDI doses to minimize inter-operator variability. The ACE, MediSpacer, and AeroVent devices were held horizontally, with the MDI in a vertical position. Both of the inline nonreservoir devices were held manually, with the 22 cm of large-bore tubing connecting to the patient Y maintained in a horizontal, approximately straight position. Inspiratory tubing upstream of the nonreservoir device was allowed to droop naturally.

Measurement of Drug All drug measures were performed by spectrophotometric assay, with a Beckman DU 640 spectrophotometer. Accuracy of wavelength was verified prior to measures using a holmium oxide filter with known wavelength pattern of absorbances. The spectrophotometer was calibrated to a baseline zero using solvent with no drug. Prior to each testing session, a standard premixed solution of either albuterol or flunisolide was sampled and the absorbance verified to determine reliability of measures. Following drug collection with albuterol, the collecting filter was washed with 20 mL of an aqueous solution of 0.4 M KH_2PO_4 (potassium phosphate, monobasic) and 0.2 M HCl (hydrochloric acid) for approximately 2 minutes with mild agitation, to dissolve the drug. Preliminary trials verified that additional drug was not recovered with a longer wash time. The sample solution was drawn up from the filter with a glass syringe, and absorbance measured at a wavelength of 276 nm. Drug concentration was calculated by linear regression fitted to serial dilutions of known albuterol concentrations with previously measured absorbances. Drug concentrations as dilute as 1 μg/mL produced absorbance readings in the second decimal place. The drug concentration was calculated for 20 mL of total solution, and averaged as a per actuation dose. Measurement of flunisolide collected at the end of the ETT was the same as for albuterol, except for the use of ethanol as a solvent. The sample solution was measured at a wavelength of 240 nm. The drug assay allowed detection of drug concentrations as low as 0.5 to 1.0 μg/mL.

Data Analysis Descriptive statistics provide the mean, standard deviation and a 95% confidence interval (CI) for dose delivery by each device. Statistical comparisons among the 5 devices for dose delivery were performed by both a nonparametric Kruskal-Wallis analysis of variance (ANOVA), as well as by a parametric one-way ANOVA, since sample sizes were small ($n = 6$, for each device).

Results

Temperature of the inspired gas in the lung model for albuterol delivery averaged 34.0° C (SD = 0.35). Table 1 gives summary statistics for the amount of albuterol delivered to the filter at the end of the ETT, expressed as a percent of the dose measured from the MDI used, for each type of MDI actuating device tested. The average MDI dose measured for albuterol from the 6 MDIs used was 87.0 ± 3.0 μg.

Table 1. Summary of dose delivery for albuterol and flunisolide at the end of the ETT for each device, expressed as a percent of the measured MDI dose. For each drug, devices are listed in order of drug delivery amount, least to greatest; devices with the same superscript (*, †, ‡) did not differ significantly from each other in dose delivery. SD = standard deviation; CI = confidence interval; n = 6 each brand

Albuterol:					
	Hudson Inline*	MiniSpacer†	AeroVent†	ACE‡	MediSpacer‡
Mean (SD)	12.0% (0.9)	17.2% (1.2)	17.7% (2.5)	30.0% (2.0)	31.8% (1.6)
95% CI	11.1–13.0%	16.0–18.5%	15.1–20.3%	27.8–32.1%	30.1–33.4%
Flunisolide:					
	Hudson Inline*	AeroVent†	ACE†	MiniSpacer†	MediSpacer‡
Mean (SD)	5.0% (0.9)	11.4% (1.8)	12.4% (2.8)	13.1% (2.2)	21.0% (1.8)
95% CI	4.0–5.9%	9.5–13.3%	9.4–15.3%	10.8–15.4%	19.2–22.8%

Analysis of variance was performed, using a significance level of 0.05 to detect differences. Both the nonparametric Kruskal-Wallis, and one-way ANOVA indicated a significant difference across brands ($p < 0.005$) for delivery of albuterol. Follow-up comparisons using the Scheffé test showed a significant difference ($p < 0.05$) between brands with different symbols in superscript (*, †, ‡), as shown in Table 1. The bidirectional MDI adaptor (MiniSpacer) delivered a larger average dose of albuterol compared to the Hudson Inline adaptor, and was equivalent to the Monaghan AeroVent, but not as efficient as the DHD ACE or the Allegiance MediSpacer.

The level of extractables from the collecting filter with the aqueous solvent was measured at 276 nm using 20 mL of solvent in a sample of filters with no drug or other substance present. The average (SD) of absorbances measured in this way with 4 filter samples was 0.0006 (0.0029). The signal-to-noise ratio, given the absorbances from the actual measured drug solutions, was calculated as 0.5% to 1.4%.

Temperature of the inspired gas in the lung model for flunisolide delivery averaged 30.6° C (SD = 0.54). Table 1 also gives summary statistics for the amount of flunisolide delivered to the filter at the end of the ETT, expressed as a percent of the dose measured from the MDI used, for each type of MDI actuating device tested. The average MDI dose measured for flunisolide was 243.9 ± 10.0 μg ($n = 6$). Both the nonparametric Kruskal-Wallis and one-way ANOVA indicated a significant difference across brands ($p < 0.005$) for delivery of flunisolide. Follow-up comparisons using the Scheffé test showed a significant difference ($p < 0.05$) between brands with different symbols in superscript (*, †, ‡), as shown in Table 1. For delivery of flunisolide, the bidirectional MDI adaptor (MiniSpacer) was equivalent to both the ACE and the AeroVent, but lower in dose delivery than the MediSpacer.

The level of extractables from the collecting filter with the ethanol solvent was measured using 20 mL of solvent in a sample of filters with no drug or other substance present. The average (SD) of absorbances measured in this way with 4 filter samples was 0.0098 (0.003). For the Hudson Inline adaptor with absorbance measures that averaged 0.1259, the average noise ratio was 7.8%. The noise level with ethanol and the collecting filter was higher than that seen with the aqueous solvent.

Discussion

Inline nonreservoir, or T-type MDI adaptors, attach to the corrugated tubing of the inspiratory limb of the ventilator circuit. This type of MDI adaptor uses the inspiratory tubing as a reservoir for the aerosol plume, since there is negligible internal holding volume to the adaptor itself. This design offers several advantages: no water or fluid accumulation, minimal weight on the circuit and ETT, and no need to open the ventilator circuit for continual insertion/removal. Due to the relatively small internal diameter of the corrugated inspiratory tubing, high inertial impaction loss could be expected, and this may be the primary mechanism for the lower aerosol delivery seen with inline nonreservoir devices. The design of the MiniSpacer provides a bidirectional spray. The aerosol released from the MDI is divided, with approximately equal portions directed into the inspiratory tubing *toward* the patient as well as *upstream* toward the ventilator. As a result of this bidirectional design, the MiniSpacer effectively doubles the holding volume for the aerosol plume. The same amount of aerosol is now contained in twice the amount of inspiratory tubing. In theory, the loss due to inertial impaction would be expected to decline, with a corresponding increase in drug delivery. The results obtained for both albuterol and for flunisolide delivery with the bidirectional MDI adaptor (MiniSpacer) supported this theoretical prediction: drug delivery increased compared to the unidirectional Hudson Inline MDI adaptor, from 12% to 17%, and from 5% to 13%, respectively, for the 2 drugs. For albuterol, the bidirectional inline adaptor delivered doses to the end of the ETT that were equivalent to the AeroVent (approximately 17% of the MDI dose), but that were lower than the dose seen with the ACE or the MediSpacer, both of which delivered approximately 30% of the MDI dose. With flunisolide delivery, the bidirectional inline adaptor was as efficient as either the AeroVent or the ACE, with all 3 devices delivering approximately 12% of the MDI dose. Again, the MediSpacer delivered a larger percentage of the MDI dose, with approximately 21% of the flunisolide dose reaching the end of the ETT.

The improved drug delivery with the increased holding volume obtained by the bidirectional aerosol spray is consistent with results previously obtained by Morén.[11] Morén measured the loss of terbutaline sulfate in actuator tubes of various lengths and diameters, as well as in a pear-shaped reservoir device. As the tube diameter increased from 24 mm to 32 mm, loss of aerosol drug decreased. The large pear-shaped reservoir, which was 250 mm in length and 130 mm in diameter at its widest point, gave the lowest aerosol loss, as would be expected. In comparison, the outside diameter of both of the inline nonreservoir devices tested in the present study were 22 mm. Morén's results support the theory that increased holding volume can reduce aerosol loss, which may be a function of inertial impaction. We suspect that this is the basis for the greater efficiency seen with the ACE and MediSpacer in the delivery of albuterol. The ACE and the MediSpacer have the greatest length and internal diameter of the 3 reservoir devices, which should theoretically minimize internal inertial impaction of the aerosol plume. This is proportionally similar to Morén's dose measures with the pear-shaped reservoir.

The results of the present study, which showed the lowest aerosol drug delivery for albuterol with the unidirectional inline nonreservoir device (Hudson Inline adaptor), are consistent with results obtained by both Fuller et al, as well as by Bishop et al. Fuller et al found that an inline nonreservoir device (the Instrumentation Industries T-type device, model not specified) delivered less drug to the lungs in vivo, than either a 700 mL or a 167 mL reservoir device.[3] The bench study by Bishop et al similarly found that an inline nonreservoir device, the Instrumentation Industries RTC-22, delivered a lower volume of particles $< 5.0\ \mu m$, as well as a lower percentage of MDI dose, compared to a Monaghan AeroChamber Inline spacer.[1] The 2 studies differed on the dose comparison between the inline nonreservoir device and a right-angle MDI adaptor placed directly on the ETT. However, this may have been due to differences in the studies, such as the placement of the inline device, use of humidified gas in Fuller's study, and in vivo versus in vitro conditions in the two studies.

In vitro delivery of albuterol with the AeroVent reservoir device, using a model of mechanical ventilation, has been reported by several investigators. Fink et al reported that 16.9% ± 2.0% of the dose of MDI albuterol was delivered through an ETT to filters on artificial "bronchi," with an AeroVent placed on the inspiratory limb proximal to the patient Y, using humidified inspiratory gas.[12] A study by Diot et al comparing the AeroVent to the Marquest MDI adaptor showed that 15.4% ± 0.2 of the nominal dose of MDI albuterol was delivered to a filter at the end of the ETT, using a model of mechanical ventilation with humidity.[13] In the study by Diot et al, the AeroVent was placed 20 cm above the Y-piece on the inspiratory limb. Both of these amounts agree closely with the 17.7% ± 2.5% for albuterol delivery with the AeroVent in our study. This degree of consistency for the AeroVent device with the previous two studies serves to corroborate the validity of the present results.

A significant result of the present study is the difference in efficiency of the same device, when delivering the β_2 agonist albuterol, and the corticosteroid flunisolide. This difference of delivery efficiency with different types of drugs has been reported in the 1995 study by Ahrens et al.[5] In general, we found that each device measured delivered a lower percentage of MDI dose with the corticosteroid flunisolide, compared to the β_2 agonist albuterol. The average dose of flunisolide across all the devices was approximately 12.6% of the MDI dose compared to 21.7% for albuterol. The percentage of albuterol MDI dose delivered at the end of the ETT ranged from 12%-32%, whereas the percentage of flunisolide MDI dose was 5%-21%, for the various devices in our study (Table 1). This represents a decrease in dose delivery for flunisolide compared to albuterol from approximately 30% to over 50%. Results of our study cannot be compared directly to those of Ahrens et al. Ahrens et al measured delivered dose from 4 brands of reservoirs using cascade impaction testing in contrast to our use of a lung model, with a biphasic breathing cycle, an ETT, humidity, and different flowrates during our inspiratory phase when drug was collected on the filter. The ACE was the only reservoir common to both studies. Despite these differences, Ahrens et al's study similarly found that with the ACE, the dose of flunisolide collected in the impactor (both throat and stages) was 17% of the total MDI dose, whereas the dose of albuterol collected was 41% of the MDI dose. This represents a 59% decrease in MDI dose delivery for flunisolide compared to albuterol. In our study, the ACE delivered 30% of the MDI dose of albuterol, but only 13.1% of the dose of flunisolide, a 56% decrease in efficiency similar to that seen by Ahrens and colleagues. Reasons for the difference in delivery efficiency for the β agonist compared to the corticosteroid are debated. A common explanation put forth is that the nozzle of the MDI canister differs in diameter between the two drugs albuterol and flunisolide. However, the actuator nozzle receptacle in both reservoir and nonreservoir MDI inline devices is universal for drug canisters. It is hypothesized that the MDI canister nozzles of different drugs will not fit exactly the same into the integral actuator receptacle, and that this may affect the particle size distribution, the respirable mass (commonly defined as particles $< 4.7\ \mu m$ for the Andersen cascade impactor) and the total drug mass delivered with different drugs. The influence of nozzle fit into the integral actuator on drug delivery would be in addition to that of the actuator geometry. The formulations of Proventil® brand of albuterol and AeroBid® brand of flunisolide differ to some extent as well. Both MDI formulations are microcrystalline suspensions. Proventil® is formulated with propellants trichloromonofluoromethane and dichlorodifluoromethane, along with oleic acid as a dispersing agent. AeroBid® incorporates the same propellants as listed for Proventil® with the addition of dichlorotetrafluorethane, and a different dispersing agent, sorbitan trioleate. Regardless of the cause(s), it is important to be aware that in vitro testing with various methodologies shows a difference in drug delivery efficiency for devices with integral actuators, when using different types of drugs. All inline MDI actuators for ventilator use currently employ integral actuators.

The in vitro results reported here support the need for an in vivo, clinical comparison of different inline MDI actuating devices, both reservoir and nonreservoir, that are commonly available for aerosol delivery with mechanical ventilation. While significant dose delivery differences are seen in bench testing, it remains to be determined whether these differences will produce significantly different clinical responses to albuterol. Detecting differences in clinical response to a corticosteroid such as flunisolide is more difficult and subject to confounding factors.

Conclusion

The new nonreservoir bidirectional MDI adaptor was superior to the unidirectional Hudson nonreservoir adaptor in dose delivery through an ETT for both albuterol and flunisolide. For delivery of albuterol, the bidirectional adaptor was equivalent to the AeroVent reservoir but not as efficient as the MediSpacer or ACE reservoirs. For delivery of flunisolide, the bidirectional adaptor was equivalent to both the ACE and the AeroVent, but lower than the MediSpacer. Delivery of the corticosteroid flunisolide was lower for all devices compared to delivery of albuterol.

PRODUCT SOURCES

Ventilator

Model MA-1, Nellcor Puritan Bennett Corp, Pleasanton CA

Test Lung

Dual adult training/test lung, Model 1600, Michigan Instruments Grand Rapids MI

Ventilator Tester

Bio-Tek adult ventilator tester, Model VT-1, Bio-Tek Instruments Inc, Winooski VT

Humidifier

Model MR 480, Fisher & Paykel Healthcare Inc, Laguna Hills CA

Spectrophotometer

Model DU 640, Beckman Instruments, Fullerton CA

Drug Collection Filter

two-way nonconductive anesthesia filter, model 43410–241, Baxter Healthcare Corp, Valencia CA.

HEPA filter

Model BB-50T, Pall Corp, East Hills NY

MDI Actuating Devices

Aerosol Cloud Enhancer (ACE)
DHD Healthcare, Canastota NY
AeroVent
Monaghan Medical Corp, Plattsburgh NY
Inline MDI Adaptor
Hudson RCI®, Temecula CA
Airlife MediSpacer and Airlife MiniSpacer
Allegiance Healthcare Corp, McGaw Park IL

Metered Dose Inhaler Drugs

albuterol (Proventil®)
Schering-Plough Corp, Kenilworth NJ
flunisolide (AeroBid®)
Forest Pharmaceuticals Inc, St Louis MO

Ventilator Circuit

Uni-Set
Dart Respiratory, Ocala FL

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Cardiac Enzyme Evidence of Cardiac Injury in Patients Intubated for Respiratory Failure

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INTRODUCTION: Patients who develop acute respiratory failure (ARF) experience multiple pathophysiologic events that can produce cardiac injury in the immediate postintubation period. Although myocardial infarction is stated to be a complication of respiratory failure, no patient series confirm this impression or describe the importance of cardiac injury in this clinical setting. METHODS: We prospectively evaluated 81 patients over 45 years old who required intubation and mechanical ventilation for ARF to determine the incidence of cardiac enzyme evidence of cardiac injury related to the initiation of mechanical ventilation, the association of elevated cardiac enzymes with clinical outcome, the clinical features that predicted the occurrence of elevated cardiac enzymes, and the cost-effectiveness of different diagnostic strategies. RESULTS: We observed that 11 of 81 patients [14%, 95% confidence interval (CI), 6–21%] had enzyme evidence of cardiac injury of whom two demonstrated new Q waves. No patient developed clinically apparent events attributable to a myocardial infarction, and enzyme elevation did not correspond to mortality. A logistic model identified patients for cardiac enzyme screening by the presence of a postintubation heart rate > 140 beats/min or a history of coronary artery disease. The model had a diagnostic accuracy of 67% (95% CI, 56–77%), sensitivity of 91% (95% CI, 59–100%), specificity of 63% (95% CI, 51–74%), positive predictive value of 28% (95% CI, 14–45%), and negative predictive value of 98% (95% CI, 88–100%). CONCLUSION: Selection of patients with noncardiac respiratory failure for cardiac enzyme evaluation by the presence of postintubation heart rate > 140 beats/min or a history of coronary artery disease is more cost-effective than screening all intubated patients. [Respir Care 1998;43(9):713–718] *Key words: acute respiratory failure, cardiac enzymes, myocardial infarction.*

Introduction

Patients with acute respiratory failure (ARF) experience profound alterations in cardiovascular function during both spontaneous and ventilator-assisted respiration.[1] Increased work of breathing (WOB), cyclic changes in intrathoracic pressure, hypoxemia, acidosis, and hypercapnia initiate complex cardiopulmonary interactions that can cause pulmonary hypertension, depressed left ventricular systolic function, decreased cardiac output, and varying degrees of systemic hypotension or hypertension.[2] Endotracheal intubation may further alter cardiovascular function by producing a sympathoadrenal response.[3–5] This response is characterized by a sudden rise in plasma concentrations of epinephrine and norepinephrine[6,7] that causes transient tachycardia and hypertension with systolic blood pressures briskly rising 35–70 mm Hg above baseline values.[8] Conditions associated with respiratory failure, such as anemia, primary arrhythmias, and systemic hypotension, add additional risks for cardiac injury.

Recent studies in critically ill patients with and without respiratory failure demonstrate that cardiac injury commonly occurs in this patient population and may contribute to mortality.[9,10] Although clinical reviews[2] state that myocardial infarction is a complication of ARF in general, to our knowledge no studies exist to define the incidence and

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outcome of cardiac ischemic events experienced in the immediate postintubation period. Despite an absence of data, we have observed that many clinicians routinely screen patients with respiratory failure with serial cardiac enzyme studies even though the respiratory failure appears clinically to be noncardiac in origin.

In this study, we prospectively studied patients with noncardiac causes of ARF who were in the age range in which they may have atherosclerotic coronary vascular disease to determine the value of postintubation screening of patients for cardiac injury. Laboratory and clinical findings were examined to estimate the incidence of elevated cardiac enzymes compatible with cardiac injury, determine the effect of elevated cardiac enzymes on clinical outcome, and develop a cost-effective strategy for evaluating patients with ARF for the occurrence of myocardial infarction.

Methods

The study was performed at a 526-bed tertiary care teaching medical center. The study protocol was approved by the Institutional Review Board. Consecutive patients ≥ 45 years old who required intubation and mechanical ventilation for noncardiac causes of respiratory failure were identified from daily admission logs and considered for study entry during the period from July 1994 to June 1997. Inclusion criteria required that patients underwent translaryngeal intubation in the emergency department or inpatient setting for respiratory failure due to one of the following disorders: chronic obstructive pulmonary disease (COPD), asthma, pneumonia, or miscellaneous noncardiac disorders that included pleural effusions, acute aspiration, pneumothorax, or upper airway obstruction. Exclusion criteria included a history of a myocardial infarction within the previous 2 months, clinical impression by the attending physician that a myocardial infarction, cardiac arrhythmia, or cardiogenic pulmonary edema caused or contributed to the respiratory failure, death within 24 hours of intubation, and failure to obtain serial creatine kinase (CK) serum assays.

Patients were intubated via the oral or nasal route and managed with intermittent mandatory or assist-control ventilatory modes with Siemens 300 and Siemens Servo 900C ventilators (Siemens-Elena AB, Solina, Sweden). An electrocardiogram (ECG) was performed immediately after intubation in all patients. Some patients received daily ECG studies for an additional 2 days at the discretion of the primary physician. Three blood samples were drawn every 12 hours beginning within 1 hour after intubation for determination of CK levels, CK-MB levels, and CK-MB index by standard laboratory methods. Vital signs and laboratory data were collected from the most proximate results before and immediately after intubation.

ECGs were read by one of the investigators (ZA) who was masked to the patient source. Interpretations were limited to the presence of myocardial ischemia, myocardial infarction, and arrhythmias. Criteria for myocardial infarction were ST segment elevation > 0.1 mV or new Q waves > 0.4 seconds in two or more contiguous leads.[11] Criteria for myocardial ischemia were ST segment depression > 0.1 mV 0.08 seconds after the J point or deep symmetric T wave inversion in two or more contiguous leads.[11] Myocardial infarction was defined by the occurrence of a CK > 200 IU/L with a CK-MB index ≥ 4%.[11]

Study patients were monitored during their entire hospitalization to detect clinical events compatible with myocardial ischemia. Monitored events included ventricular arrhythmias, anginal chest pain, cardiac arrests, new onset congestive heart failure, and new or recurrent myocardial infarctions.

The cost-effectiveness of different diagnostic strategies was calculated from charge data at our institution for the individual tests: CK $24.42, CK-MB $17.76, CK-MB index $16.65, and ECG $122.04. Analyses were recalculated on the basis of actual costs. Results were calculated by multiplying the total charges or costs of an evaluation strategy by the number of patients who would receive screening in various screening strategies. The product was then divided by the number of patients determined by the study to have cardiac injury. Results were expressed both as charges or costs per myocardial infarction detected. We performed a sensitivity analysis on both the charge and cost economic analyses by varying the incidence of cardiac injury within its observed 95% confidence intervals (CIs) for our study population.

Categorical variables were analyzed by the χ^2 test or the 2-tailed Fisher exact test when appropriate. Simple logistic regression determined the effect of continuous variables on categorical outcomes. Multiple logistic regression was used to determine independent predictors of myocardial infarction. Explanatory variables in the univariate analysis with p values < 0.1 were entered into the logistic model in a forward stepwise manner and removed if their p values were ≥ 0.05. Postintubation vital signs and laboratory values were used for the logistic model. Correlations between explanatory variables were assessed by calculation of Pearson product-moment correlation coefficients.[12] Continuous variables were transformed to dummy variables by dichotomizing with cutoff values determined by receiver operating characteristic (ROC) analysis.[13] Cutoff values were selected at points on the ROC curve closest to 100% sensitivity and 100% specificity. CIs were calculated using the exact method. All data analyses were performed with JMP statistics software version 3.1 (SAS Institute, Cary NC) on a personal computer (Macintosh 8500/80).

Table 1 Characteristics of the Patients and Distribution of Myocardial Infarction (MI) within Patient Characteristics

Variable	No. of Patients (%)	No. (%) with MI [95% CI*]	Odds Ratio (95% CI) for MI	p Value†
All patients	81 (100)	11 (13.6) [7.0–23.0]	–	–
Men	34 (42)	6 (17.7) [6.8–34.5]	1.8 (0.5–6.8)	0.5
Women	47 (58)	5 (10.6) [3.6–23.1]	0.6 (0.1–2.0)	0.5
Cause of respiratory failure				
COPD	25 (31)	5 (20.0) [6.8–40.7]	2.1 (0.5–7.7)	0.3
Asthma	3 (4)	0 (0) [–]	–	1.0
Pneumonia	41 (50)	4 (9.8) [2.7–23.1]	0.5 (0.1–1.8)	0.3
Other	12 (15)	2 (16.7) [2.1–48.4]	1.3 (0.2–6.2)	0.7
History of coronary artery disease	20 (25)	7 (35.0) [15.4–59.2]	7.7 (2.0–33.2)	0.004
History of myocardial infarction	13 (16)	5 (38.5) [13.9–68.4]	6.5 (1.6–26.8)	0.013
Route of intubation				
Oral intubation	46 (57)	3 (6.5) [1.4–17.9]	0.2 (0.0–0.9)	0.049
Nasal intubation	35 (43)	8 (22.9) [10.4–40.1]	4.2 (1.1–20.7)	0.049
Preintubation arrhythmias	26 (32)	5 (19.2) [6.6–39.4]	1.8 (0.5–6.6)	0.5

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*CI = confidence interval, COPD = chronic obstructive pulmonary disease.

†p value pertains to the univariate analysis of explanatory variables for the presence of a myocardial infarction.

Results

Ninety-one consecutive patients with ARF who fulfilled the inclusion criteria were entered into the study. Ten patients were excluded from analysis for the following reasons: 2 patients died within 24 hours of intubation, and 8 patients did not undergo CK blood assays because they missed blood draws while in radiology for imaging procedures. The median age of patients was 70 years (interquartile range, 61–77 years, range 45–90 years). The clinical features of the 81 evaluable patients are shown in Table 1.

Eleven of the 81 patients (14%, 95% CI, 6–21%) fulfilled the study definition of myocardial infarction. The results of the 3 serial CK and CK-MB assays obtained 12 hours apart in all 81 of the study patients are shown in Table 2. Eight of the 11 patients with cardiac injury first fulfilled CK criteria for myocardial infarction by the first CK determination, 2 patients fulfilled CK criteria by the second CK determination, and 1 patient fulfilled CK criteria by the third CK determination.

Table 2 Results of Creatine Kinase (CK), Creatine Kinase Isoenzyme (CK-MB), and CK-MB Index Assays

	CK (IU/L)	CK-MB (IU/L)	CK-MB Index (%)
First assay* (n = 81)			
Median	528	3.6	4.2
Interquartile range	240–1228	1.5–9.0	3.5–5.8
Range	125–1306	0.4–82	1.9–8.6
Second assay (n = 81)			
Median	536	3.6	3.4
Interquartile range	221–1161	1.7–8.2	2.1–4.2
Range	123–1840	0.4–63.8	1.5–6.5
Third assay (n = 81)			
Median	205	3.0	2.5
Interquartile range	69–388	1.3–8.8	2.1–3.6
Range	15–5140	0.4–91.2	1.9–12.1

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*Assays performed at 12-hour intervals

Table 1 shows the distribution of myocardial infarctions among categorical demographic and clinical variables. Among these variables, a history of coronary artery disease, history of a previous myocardial infarction, and route of intubation were positive predictors in the univariate analysis for postintubation myocardial infarction. Age was not an explanatory variable for myocardial infarction ($p = 0.20$). Patients' vital signs and laboratory results were examined as explanatory variables for myocardial infarction (Table 3). Statistically significant predictors included diastolic hypertension, tachypnea, tachycardia, a postintubation ECG showing ischemia, and a postintubation ECG showing a myocardial infarction. Odds ratios using categorical and dummy variables are shown for variables with $p < 0.1$ and were entered in the multivariate analysis.

Mean arterial pressure was not entered into the logistic model because it correlated with diastolic hypertension (correlation coefficient 0.91; $p < 0.0001$). Among the explanatory variables in Tables 1 and 3 with $p < 0.1$, independent predictors for myocardial infarction were tachycardia > 140 beats/minute (AOR = 19.4, 95% CI, 3.0–382.0; $p = 0.008$) and history of coronary artery disease (AOR = 25.2, 95% CI, 4.0–492.2; $p = 0.004$).

Table 3 Vital Signs and Laboratory Findings of Patients, with Results of Univariate Analysis

Variable	Median (Interquartile Range) [Range]	Cutoff Value	Odds Ratio (95% CI*) for Myocardial Infarction	p Value
Preintubation values				
Systolic blood pressure (mm Hg)	130 (104–158) [36–266]	–	–	0.17
Diastolic blood pressure (mm Hg)	68 (56–84) [0–150]	–	–	0.12
Mean arterial pressure (mm Hg)	89 (73–107) [26–189]	–	–	0.12
Heart rate (beats/min)	120 (103–140) [54–161]	–	–	0.22
Respirations (breaths/min)	25 (18–36) [6–52]	>25	6.0 (1.4–41.3)	0.05
P_{aO_2} (mm Hg)	67 (54–94) [37–361]	–	–	0.88
P_{aCO_2} (mm Hg)	57 (38–85) [27–124]	–	–	0.93
pH	7.26 (7.18–7.37) [6.96–7.53]	–	–	0.78
Postintubation values				
Systolic blood pressure (mm Hg)	120 (90–146) [40–199]	–	–	0.2
Diastolic blood pressure (mm Hg)	60 (52–72) [0–107]	>65	3.8 (1.0–15.9)	0.03†
Mean arterial pressure (mm Hg)	82 (68–93) [20–138]	>85	5.5 (1.4–26.7)	0.059†
Heart rate (beats/min)	123 (98–141) [62–188]	>140	5.3 (1.4–21.0)	0.012†
Respirations (breaths/min)	20 (16–24) [10–60]	–	–	0.4
P_{aO_2}/F_{IO_2} (mm Hg)	190 (134–334) [44–564]	–	–	0.39
P_{aCO_2} (mm Hg)	42 (35–53) [21–85]	–	–	0.58
pH	7.35 (7.29–7.44) [7.13–7.56]	–	–	0.69
ECG ischemia (n = 7)	–	–	6.0 (1.0–32.5)	0.052
ECG infarction (n = 5)	–	–	12.6 (1.8–107.2)	0.017

*CI = confidence interval; ECG = electrocardiogram

†Cutoff points and odds ratios calculated for variables with p = <0.1. p values calculated from the continuous variable data.

A prediction model was developed using tachycardia > 140 beats/minute and a history of coronary artery disease. The presence of either variable significantly increased the probability of a postintubation myocardial infarction (OR 16.9, 95% CI 3.0–319.5; p = 0.0087). The overall diagnostic accuracy of the model was 67% (95% CI, 56–77%), sensitivity 91% (95% CI, 59–100%), specificity 63% (95% CI, 51–74%), positive predictive value 28% (95% CI, 14–45%), and negative predictive value 98% (95% CI, 88–100%).

Ten of the 11 patients with enzyme evidence of myocardial infarction and 26 of the 70 patients without myocardial infarction had at least one of the predictive variables of the model; 3 of the 81 study patients had both variables and all 3 of these patients had a myocardial infarction. The economic analysis found that a strategy of ruling out a myocardial infarction with 3 serial ECG studies and cardiac enzymes in all 81 of the study patients would have a charge basis of $3,996 and a cost basis of $894/myocardial infarction. Screening all 81 patients with serial cardiac enzymes and performing serial ECG studies only on those patients with abnormal enzymes would amount to charges of $1,666 and costs of $478/myocardial infarction. The prediction model would have a charge basis of $944 and cost basis of $249/myocardial infarction detected if only patients with elevated enzymes underwent serial ECG studies. Considering the sensitivity analysis, the model would decrease charges by $722 (95% CI, $472-$1826) and costs by $229 (95% CI, $145-$571) per myocardial infarction compared to a routine CK screening strategy with ECG evaluations performed on patients with abnormal CK tests.

Six of the 11 patients with myocardial infarctions had serial ECG studies; 2 of these 6 patients evolved Q wave infarctions. None of the 81 patients developed clinical events during their hospitalizations, such as chest pain or ventricular arrhythmias, suggestive of ongoing or recurrent myocardial ischemia. Twenty-three patients died with deaths occurring a median of 12 days (interquartile 6–17 d, range 2–29 d) after intubation. None of the deaths appeared related to a myocardial event. Three of the 11 patients with enzyme evidence of myocardial infarction died; none of these deaths appeared to be a consequence of myocardial ischemia. In-hospital death was not more common in the group of patients with myocardial infarction (OR = 0.9, 95% CI 0.2–3.6, p = 1.0).

Discussion

The present study demonstrates that elevated serum CK isoenzymes compatible with acute cardiac injury occur in 14% (95% CI, 6–21%) of patients with noncardiac causes of ARF. It could not be established that enzyme evidence of cardiac injury affected clinical outcome. Of the 6 patients with elevated CK isoenzymes who had serial ECG studies, only 2 evolved Q wave infarctions. None of the 81 patients had clinically apparent symptoms or signs of myocardial infarction, such as chest pain, ventricular arrhythmias, or new onset cardiac dysfunction. And none of the 23 deaths appeared to be a direct consequence of cardiac events. We also observed that clinical features could identify the at-risk patient in that the logistic model established post-intubation heart rate > 140 beats/min and a history of coronary artery disease as independent predictors of elevated cardiac enzymes (OR 16.9, 95% CI 3.0–319.5; p = 0.0087).

It should be emphasized that the study was not designed to determine the incidence of cardiac injury throughout the entire hospitalization for ARF. The use of cardiac enzyme screening during the first 24 hours after intubation may have underestimated the in-hospital incidence of cardiac injury by failing to detect myocardial infarctions that occurred later in the hospital stay subsequent to cardiac stresses unrelated to the initiation of mechanical ventilation. We considered, however, that the greatest degree of cardiac stress would most likely occur around the time of intubation when the work of spontaneous breathing had progressed to its maximum duration and severity, the brisk adrenosympathetic response to intubation had completed its course,[3–5] and patients were undergoing the sudden physiologic adaptations required to shift from spontaneous breathing to positive pressure assisted ventilation. Moreover, nonrespiratory complications frequently occur in patients intubated for ARF, which can present myocardial stress resulting in cardiac injury; other studies have previously examined the incidence of cardiac injury in patients with general categories of critical illness.[9,10] For these reasons, we designed our study to define the incidence of cardiac injury in patients with respiratory failure within the immediate postintubation period.

Conversely, the study may have overestimated the true incidence of cardiac injury because of potential noncardiac sources of CK-MB.[14,15] This overestimation would have been negligible, however, because of our definition of a myocardial infarction, which required a CK index > 4%. Injury to noncardiac tissue sources of CK-MB, such as skeletal muscle and bowel, rarely increase the CK-MB index above 1 to 2%.[16,17] Moreover, none of the study patients had rhabdomyolysis, chronic myopathies, bowel injuries, or renal failure, which are the most common causes of false positive results with CK-MB testing for myocardial infarction.[18] However, future studies with more specific markers of cardiac injury, such as troponin I[18] which was not clinically available in our hospital at the time of our study, will be required to more precisely estimate the incidence of cardiac injury after intubation for respiratory failure. It is doubtful, however, that the use of troponin I would have significantly altered our study results. CK-MB and troponin I assays have similar sensitivities for cardiac injury.[19] Although troponin I has greater overall specificity, the absence of clinical factors in the study sample associated with false positive CK-MB results makes the increased specificity of troponin I less likely to produce an increased diagnostic accuracy compared to CK-MB.

The observed 14% incidence of elevated cardiac enzymes compatible with cardiac injury is similar to the incidences noted in other studies of general populations of critically ill patients.[9,10] Guest and co-workers[10] evaluated consecutive patients admitted to a medical intensive care unit (ICU) and noted a 15% incidence of cardiac injury as evidenced by elevated troponin I serum concentrations. In a similar study, Kollef and associates[9] screened critically ill medical patients with daily troponin I assays and observed that 15.8% of patients had elevated cardiac enzyme levels.

Our investigation extends these previous observations by studying a population limited to patients who had noncardiac causes of respiratory failure as the primary reason for intubation and did not have clinical evidence of other organ dysfunction. Also, our cohort evaluated patients with an age range that put them at risk for athersclerotic cardiovascular disease. On the basis of these observations, it appears that ARF presents risks for cardiac injury that are similar to other medical causes of critical illnesses. The etiology of this injury is uncertain but may relate to imbalances between myocardial oxygen supply and demand that occur during critical illness.[20,21]

Our data do not indicate that elevated cardiac enzymes correspond with clinical outcome in patients with ARF. None of the patients had clinically apparent evidence of acute cardiac decompensation, and mortality was not higher in patients with CK enzyme elevations. This observation differs from the findings of Guest and co-workers[10] who observed a higher mortality in critically ill patients with elevated troponin I levels. These investigators, however, did not perform multivariate analyses to determine the effects of covariates on clinical outcome. Kollef and coworkers[9] determined that elevated troponin I levels in patients with clinical evidence of cardiac dysfunction were associated with increased mortality in their univariate analysis. When examined by multivariate analysis, however, elevated cardiac enzymes in the absence of acute or chronic cardiac dysfunction were not independent predictors of clinical outcome. The presence of clinically apparent cardiac dysfunction was observed to increase mortality. No patients in our study group demonstrated acute decompensation of cardiac function after intubation, suggesting that isolated cardiac enzyme elevations in ARF, as in general critical illnesses, may not alter clinical outcome. A larger population of patients with ARF should be studied to confirm this conclusion.

In devising a strategy for evaluating patients with respiratory failure for cardiac injury, it could be argued that CK should not be measured because enzyme elevations by themselves do not alter clinical outcome. We suggest, however, that selected patients should undergo screening for cardiac injury because the small number of patients with elevated CK in our study (n = 11) does not allow characterization of the clinical importance of this finding. Furthermore, elevated CK levels may alter clinical outcomes that were not assessed in this study. For instance, Chatila and co-workers[22] demonstrated that 6% of ventilator-dependent patients demonstrate ECG evidence of cardiac ischemia, which is a significant risk factor for weaning failure. The detection of enzyme evidence of cardiac injury post-intubation may alter approaches to weaning or allow more accurate assessments of complications of mechanical ventilation, such as sudden hypoxemia or hypotension that may be related to acute cardiac decompensation.

The economic assessment does not support routine cardiac enzyme screening for all patients undergoing intubation for ARF because of the high cost of this approach. The logistic model demonstrated that patients could be selected for screening with an acceptable diagnostic accuracy and high negative predictive value by the presence of a post-intubation heart rate > 140 beats/min or a history of coronary artery disease. Selecting patients for CK screening by the logistic model decreased the charges by $722 (95% CI, $472-$1826) and costs by $229 (95% CI, $145-$571) per patient with myocardial infarction. Costs would be higher with the addition of troponin assays to the diagnostic evaluation. Larger studies assessing multiple clinical outcomes will be required to validate the model and establish its diagnostic precision. Other approaches for selecting critically ill, intubated patients for cardiac enzyme screening, such as by symptoms of chest pain or ECG changes, are problematic because of their impaired perceptive abilities, the atypical presentation of coronary insufficiency,[23] and the frequency of nonspecific ECG changes during critical illness.[24]

Conclusion

In conclusion, 14% of patients older than 45 years with ARF demonstrated CK-MB evidence of cardiac injury after intubation. The finding of an elevated CK-MB, however, did not alter the clinical outcomes assessed. The presence of a postintubation heart rate > 140 beats/min or a history of coronary artery disease identified a patient subgroup that had a high yield from CK screening. Screening patients for cardiac ischemia with these findings was more cost-effective than routine screening of all patients > 45 years of age with noncardiac respiratory failure.

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The Rationale for Respiratory Care Protocols: An Update*

James K Stoller MD

Respiratory care protocols, also called therapist-driven protocols and patient-driven protocols, are structured guidelines for respiratory therapies that are implemented, adjusted, and discontinued by respiratory care practitioners (RCPs) under physician oversight.[1] Such protocols, which address a broad range of respiratory services, are in widespread use currently, with available data suggesting continuing adoption. Indeed, polls of American Association for Respiratory Care (AARC) House of Delegates attendees[2] and of attendees of the 1995 California Society of Respiratory Care[1] showed that even three years ago, protocols were used in 41% to 50% of respondents' institutions and were due to be implemented in an additional 15% to 42%. Further evidence of growing interest regarding respiratory care protocols is the popularity of lectures and courses regarding the content and application of respiratory care protocols. [3]

In the context of this widespread enthusiasm, this article first considers the rationale for protocols and then reviews available studies evaluating their impact. The current article updates an earlier review of these issues[1] and emphasizes studies reported since that earlier publication. Because the current paper is a sequel, some issues that were discussed in detail in the earlier paper and for which little new information has become available are presented at most briefly. Examples include discussions of the reasons for misallocation and data regarding over-ordering of some specific respiratory care treatments, such as bronchodilators.

Misallocation of Respiratory Care: Frequency and Types

The main impetus for respiratory protocols is to enhance appropriate prescription of respiratory care services and/or to minimize misallocation, which has been shown to occur commonly in many types of health care institutions and for a broad range of respiratory care services. Table 1 summarizes available studies reporting misallocation of respiratory care, [4-11] which consists both of "over-ordering" and of "under-ordering" respiratory care. Most studies focus on "over-ordering" (ie, ordering services that are unlikely to provide clinical benefit), the frequency of which ranges from 25% (for 5 respiratory care services examined by Kester and Stoller[7]) to 61% for bronchopulmonary hygiene. [9,10] Studies published since the earlier review show similar rates of misallocation. For example, in an examination of bronchopulmonary hygiene ordering at University of California Los Angeles (UCLA) Medical Center, Alexander et al[10] reported that orders for 59.6% of patients examined were deemed inappropriate. This rate closely resembles the rate of 61% reported nine years earlier by Shapiro et al[9] (Table 1).

Under-ordering of respiratory care services, defined as failing to provide beneficial treatments, is more difficult to measure and has received less attention. However, two studies[7,8] have reported the frequency of under-ordering respiratory care services. Specifically, Albin et al[8] examined oxygen ordering practices at the University of Maryland and reported 20% under-ordering in 274 patients studied. The ordering consisted both of failing to prescribe any oxygen for patients whose oxygen saturation as measured by pulse oximetry S_{pO_2} was $< 92\%$ and of failing to prescribe oxygen in sufficient liter flow rates to assure adequate saturation values (which occurred in 7% of instances). This second type of under-ordering suggests inadequate attention or knowledge of appropriate physiologic end points, which is one of the reasons underlying misallocation of respiratory care services.

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In a second study of under-ordering of respiratory care services at The Cleveland Clinic Foundation, we reported an overall rate of 10.5% of under-ordering for 5 respiratory care treatment types.[7] Rates of under-ordering ranged

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Table 1 Frequency of Misallocation of Respiratory Care Services in Selected Series

Types of Service	Author(s)	Date	Patient Type	N	Frequency of Over-ordering	Frequency of Under-ordering
Supplemental oxygen	Zibrak et al	1986	Adult	NS	55% reduction in incentive spirometry after therapist supervision begun	NA
	Brougher et al	1986	Adult, non-ICU inpatients	77	38% ordered to receive O_2 despite adequate oxygenation	NA
	Small et al	1992	Adult, non-ICU inpatients		72% of those checked had $PaO_2 > 60$ mm Hg or $SaO_2 > 90\%$ but were prescribed oxygen	NA
	Kester and Stoller	1992	Adult, non-ICU inpatients	230	25.2% overall for 5 respiratory care services; 28% for supplemental oxygen	10.5% overall for 5 respiratory care services, 8% for supplemental oxygen
	Albin et al	1992	Adult, non-ICU inpatients	274	61% ordered to receive supplemental oxygen despite $SaO_2 \geq 92\%$	21% under-ordered, including 19% prescribed to receive inadequate O_2 flow rates
Bronchial hygiene techniques	Zibrak et al	1986	Adult	NS	55% reduction in incentive spirometry after therapist supervision begun	NA
	Shapiro et al	1988	Adult, non-ICU inpatients	3400	61% reduction of bronchial hygiene after system implemented	NA
	Kester and Stoller	1992	Adult, non-ICU inpatients	230	32%	8%
	Alexander et al	1996	Adult, inpatients	177	59.6% over-ordering	NA
Bronchodilator therapy	Zibrak et al	1986	Adult	NS	50% reduction in aerosolized medication after therapist supervision begun	
	Kester and Stoller	1992	Adult, non-ICU inpatients	230	12%	12%
Intermittent positive pressure breathing (IPPB)	Zibrak et al	1986	Adult	NS	92% reduction in IPPB after therapist supervision begun	NA
	Kester and Stoller	1992	Adult, non-ICU inpatients	230	40%	6.7%
Arterial blood gases	Browning et al	1989	SICU patients	724 ABGs	42.7% inappropriately ordered before guidelines implemented	NA
	Pilon et al	1997	Adult, inpatients in 5 periods	150 patients	56% inappropriately ordered before guidelines, reduced to 21% inappropriate 13 months after	NA

NA - Not assessed
NS - Not stated

from 4.0% for incentive spirometry to 12.0% for aerosolized bronchodilators in this study.

In summary, available evidence suggests the following conclusions:

1. Misallocation of respiratory care services is common, and occurs in many types of health care institutions (eg, adult and pediatric, academic and private) and for a variety of respiratory care services.

2. Both over-ordering and under-ordering occur. Although over-ordering seems more common, the paucity of available studies and the sampling frames considered suggest that reported frequencies of under-ordering are underestimates.

Possible Reasons for Misallocation of Respiratory Care Services

Understanding the reasons that misallocation occurs can suggest strategies to lessen misallocation. Though sparsely studied, three possible reasons have been proposed:

1. Respiratory care conditions are frequently misdiagnosed, leading to the prescription of inappropriate therapies.

2. Respiratory care treatments are prescribed more cavalierly than drugs, with inadequate attention to appropriate dose and frequency.

3. Health care providers who are empowered to order respiratory care services lack appropriate knowledge about

underlying principles to make optimal prescribing decisions.

Although all three factors undoubtedly contribute to the frequency of misallocation, most attention has focused on the second and third factors. For example, Small et al[6] showed that respiratory care services were ordered and implemented less precisely than orders for intravenous (I.V.) antibiotics. In their study of 96 recipients of oxygen and 60 recipients of I.V. antibiotics, errors in prescribing oxygen (eg, inappropriate prescription of route, liter flow, or duration) were more common (up to 58%) than errors in ordering antibiotics (2%). As an example of respiratory diagnostic testing that is dissociated from clinical response, Bowton et al[12] showed that, although continuous oximetry was ordered frequently to monitor hospitalized adults, oximetric detection of hypoxemia prompted a clinical response (eg, providing supplemental oxygen or adjusting liter flow) in fewer than 26% of instances.

Inadequate knowledge of respiratory care services by those empowered to prescribe is a major concern and has been demonstrated in several studies.[13,14] For example, two studies testing physicians' and nurses' knowledge of pulse oximetry show high error rates on responses to simple questions regarding principles of oximetry assessment in prescribing. Specifically, Rodriquez et al[13] administered a 16-item questionnaire to pediatric house officers in 4 institutions and recorded a mean correct rate of 64%. Notably, 34% of respondents thought that pulse oximeters measured transcutaneous oxygen tension (tcP_{O_2}) rather than percent hemoglobin saturation. More recently, Stoneham et al[14] administered a questionnaire to 30 British house officers and to 30 practicing nurses to ascertain responses to the following questions: (1) What does pulse oximetry measure? (2) How does it work? (3) What factors affect the accuracy of saturation readings? and (4) How much training regarding pulse oximetry did you receive? The responses indicated poor knowledge about pulse oximetry with 30% of physicians and 95% of nurse respondents indicating that pulse oximetry measured partial pressure or content of oxygen. Ten percent of physicians and 7% of nurses indicated that pulse oximetry measured respiratory rate or tidal volume (V_T) and 97% of respondents in both groups were unaware that pulse oximetry required pulsatile flow. Finally, only 1 of 30 physicians reported receiving specific training about pulse oximetry.

Overall, though sparse, available studies do suggest that respiratory care services are prescribed cavalierly and that those ordering respiratory care services lack adequate knowledge about these modalities. In the context of these two explanations for misallocation, two strategies for lessening misallocation are suggested. First, attention to both training health care providers about respiratory care services and to assuring their adequate understanding is needed. Second, by empowering trained RCPs to order respiratory care services under physician guidelines, protocols represent another strategy to enhance the allocation of respiratory care.

Evidence that Use of Respiratory Protocols Lessens Misallocation of Respiratory Care Services

As cited in the earlier review,[1] studies published through 1994 regarding the efficacy of respiratory protocols were relatively few and consisted of observational studies. Notwithstanding these methodological limitations, several earlier studies are noteworthy. For example, Browning et al[15] reported that implementing guidelines for ordering arterial blood gases (ABGs) in a surgical intensive care unit (ICU) was associated with lowering the rate of inappropriately ordered ABGs from 42.7% to 32.9% one month later. Also, compared to other health care providers, RCPs were more likely to abide by guidelines and therefore more likely to order ABGs appropriately.

Also, Hart et al[16] conducted a 12-week crossover study in which RCPs initially interacted with internists but not with surgeons regarding orders for intermittent positive pressure breathing and medicated aerosols. During the second 6-week study arm, therapists interacted with surgeons but not with internists. The results of this study showed that RCP interaction was associated with a lower rate of inappropriate orders for these modalities of respiratory care.

More recent observational studies confirm the effectiveness of protocol-guided respiratory therapies to enhance the allocation of respiratory care services. For example, revisiting the issue of ABG utilization in the ICU, Pilon et al[11] reported that implementing a guideline (that was drafted by a multidisciplinary group) for ABG ordering was associated with a progressively decreasing number of ABGs/patient/d (from mean 4.9 to 3.1 at 2–3 mo), while the percentage of appropriately sampled ABGs rose from a mean of 44% to 79–80%. This favorable impact on appropriateness persisted for at least 13 months after guideline implementation, and these benefits were achieved with substantial savings ($40,175 Canadian over 1 year) and with no measurable adverse effects on ICU mortality, ventilator-days, or time to wean from mechanical ventilation.

In a prospective observational study at The Cleveland Clinic Foundation, Komara and Stoller[17] examined the impact of a respiratory care protocol for titrating and discontinuing supplemental oxygen in patients undergoing general, urologic, and orthopedic surgery. The protocol, which called for discontinuing supplemental oxygen when the patient's room air pulse oximetry saturation was stable and exceeded 92%, was implemented by respiratory therapists at physician discretion. Comparing the use and true costs of oxygen monitoring and the duration of postoperative oxygen therapy in a convenience sample of 20 patients whose oxygen was adjusted by the managing physicians versus 20 patients for whom the physicians requested respiratory therapists' use of the algorithm, use of the protocol was associated with significantly shortened duration of oxygen use (mean 2.10 vs 3.45 d, $p < 0.003$), decreased oximetry measurements before discontinuation of oxygen (mean 1.2 vs 2.9, $p < 0.003$), and cost savings of approximately $21/patient.

Although the savings accrued in the 20 protocol-managed patients was very modest (approximately $428), extrapolation of these per patient savings to the 12,119 oxygen-using inpatients at The Cleveland Clinic Hospital in 1995 projected an annual savings of $263,346.

In a more comprehensive assessment of the impact of a respiratory care protocol service, Stoller et al[18] compared the pattern and appropriateness of ordering respiratory care by a Respiratory Therapy Consult Service (RTCS) versus ordering by managing physicians. The convenience sample of 98 adult inpatients consisted of 51 patients whose physicians elected RTCS-directed respiratory care and 47 patients whose respiratory care was physician-directed.

Patients for whom the RTCS was requested (RTCS group) had a greater severity of respiratory illness based on having a lower Triage Score, [19] but the compared groups were otherwise similar at bedtime. Using algorithm-based respiratory care determined by a study investigator as a "standard care plan," fewer initial orders for respiratory care were discordant with the standard care plan in RTCS patients (15% ± 26% [SD]) than in non-consult patients (43% ± 36%, $p < 0.001$), and a smaller fraction of RTCS patients received at least one discordant initial respiratory care order (37% vs 72%, $p < 0.001$). Although provided to sicker patients with longer lengths of hospital stay, RTCS-directed care generated similar respiratory care costs per patient ($335.63 ± $272.69 [RTCS] vs $349.06 ± $273.27, $p = 0.72$). Taken together, the results of these studies suggest that respiratory care protocols implemented by a RTCS can be an effective strategy to enhance the allocation of respiratory care services while conserving costs. However, as in the aforementioned study, because the observational nature of the study design neither assured nor achieved baseline similarity of the RTCS and physician-directed care groups, these results do not discount the possibility that the RTCS was associated with a longer length of stay.

To address this methodological reservation, a randomized trial of RTCS versus physician-directed respiratory care has been conducted. Specifically, Stoller et al[20] conducted a randomized controlled trial in which eligible subjects were adult non-ICU inpatients whose physicians had prescribed specific respiratory care services. Consecutive eligible patients were approached for consent, after which a blocked randomization strategy was used to assign patients to physician-directed respiratory care (in which the prescribed physician orders for respiratory care services were maintained [n = 74]), or to RTCS-directed respiratory care (in which the physician's respiratory care orders were pre-empted by an RTCS-generated care plan [n = 71]). As in the earlier observational study, [18] these patients were evaluated by an RTCS therapist evaluator, whose respiratory care plan used sign/symptom-based algorithms that were drafted to comply with AARC Clinical Practice Guidelines.* Appropriateness of respiratory care orders was again assessed as agreement between the prescribed care plan and an algorithm-based "standard care plan" generated by an expert therapist who was blind to the actual patient orders. The study results showed that the compared groups were similar at baseline regarding demographic features, admission diagnostic category, smoking status, and, unlike the prior observational study, with Triage Score (mean 3.8 ± 0.9 [RTCS] vs 3.7 ± 1.0) as well. Similarly, no differences were observed between RTCS-directed and physician-directed respiratory care regarding hospital mortality rate (5.7% vs 5.6%), mean hospital length of stay (7.9 ± 9.0 vs 7.7 ± 7.3 d), total number of respiratory care treatments delivered per patient (30.0 ± 30.0 vs 31.6 ± 30.5), or days requiring respiratory care services (4.2 ± 5.2 vs 4.1 ± 3.6). Notably, using both a stringent and a liberal criterion for agreement, RTCS-directed care demonstrated better agreement with the "standard care plan" (82 ± 17% [stringent] and 86 ± 16% [liberal]) than did physician-directed respiratory care (64 ± 21% [stringent] and 72 ± 23% [liberal], $p < 0.001$). In multivariate logistic regression models fit for predicting perfect agreement with the "standard respiratory care plan," randomization group, gender, and admitting diagnosis category achieved significance. Adjusting for gender and admitting diagnosis category, the odds of reaching perfect agreement using the stringent criterion were 6.9 times higher for RTCS-directed respiratory care than for physician-directed care (95% confidence interval [CI] 2.4 - 20) and 3.4 times higher using the liberal criterion (95% CI 1.5 - 7.6). Finally, the true cost of respiratory care treatments was slightly lower with RTCS-directed respiratory care (mean $235.70 vs $225.70/patient, $p = 0.61$). In summary, the randomized controlled trial addressed the methodological shortcomings of the earlier observational study and showed that compared to physician-directed respiratory care, the RTCS prescribed a similar number and duration of respiratory care services at a slight savings and without any increased adverse events. Also, Respiratory Therapy Consult Service-directed respiratory care showed greater agreement with Clinical Practice Guidelines-based algorithms, suggesting decreased misallocation of respiratory care services.

To the extent that carefully performed randomized controlled trials represent the preferred design to rigorously evaluate the efficacy of respiratory care protocols, such supportive results from such randomized trials provide a compelling endorsement for respiratory care protocols. To my knowledge at this writing, one other randomized trial of a respiratory care protocol has been reported and also demonstrates efficacy. Specifically, in assessing protocol-guided weaning from mechanical ventilation, Kollef et al[21] randomly allocated 357 patients in 4 ICUs to physician-directed weaning (n = 178) versus weaning by a respiratory therapist/nurse-implemented protocol (n = 179). Observed benefits of protocol-guided weaning included a shorter duration of mechanical ventilation (mean 69.4 vs 102 h, $p = 0.029$), a trend toward shorter duration before the start of weaning (mean 39.6 vs 58.3 h, $p = 0.16$), and a cost savings of $42,960 associated with protocol use. No differences were observed between the compared groups (protocol vs physician-directed weaning) regarding the need for mechanical ventilation for > 7 days, reintubation rate (12.8% vs 10.1%), hospital mortality rate (22.3% vs 23.6%), or mean hospital length of stay (12.7 vs 14.2 d). Overall, this randomized controlled trial demonstrated that the use of weaning protocols implemented by nurse and respiratory care practitioners can accelerate weaning and lessen costs without adverse clinical consequences.

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*The American Association for Respiratory Care. Clinical Practice Guidelines. Respir Care 1996; 41(7):628.

Summary and Future Directions

In summary, the results of available studies suggest that misallocation of respiratory care services occurs commonly and that respiratory care practitioner-implemented protocols for respiratory care services can lessen misallocation without increasing the cost of care or adverse clinical outcomes. Although the results of many observational studies and of two randomized controlled trials suggest that respiratory care protocols have efficacy, further study is needed to strengthen endorsement for respiratory care protocols.[22] Specifically, confirmatory studies regarding weaning and adult non-ICU inpatient care are needed, as are studies addressing the impact of respiratory care protocols in a broader spectrum of clinical settings (eg, pediatric care, subacute, and extended care) and involving a broader spectrum of respiratory care services. Also, greater attention must be paid to whether protocols hamper or help physicians'-in-training learning about respiratory care or whether protocols affect trainees' attitudes toward caring for the whole patient. Finally, studies comparing alternative strategies for enhancing allocation of care, such as respiratory care protocols versus intensive training of health care providers, are needed to clarify the true role of respiratory care protocols and the settings in which their impact can be optimal.

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Lung Protective Ventilatory Strategies for ARDS—the Data Are Convincing!

Over the past decade, experimental studies (reviewed in Ref 1) provided unequivocal evidence that the use of large inflation volumes and pressures induces a high permeability-type pulmonary edema. It has repeatedly been demonstrated that this ventilator-induced lung injury is due to large end-inspiratory volumes rather than high airway pressures; thus the resulting injury should be termed "volutrauma" rather than "barotrauma."[1] On the other hand, many investigators reported that ventilation with low end-expiratory lung volume was also associated with worsening of lung injury.[2,3] The use of positive end-expiratory pressure (PEEP) to keep end-expiratory lung volume above the lower inflection point (LIP) of the static pressure-volume (P-V) curve and to avoid permanent collapse of the alveoli seems to exert a protective effect.[2] This protective effect may also result from reduced cyclic lung stretch and hemodynamic alterations.[1]

Ventilatory Objectives

In the light of the points raised above, ventilatory objectives in acute respiratory distress syndrome (ARDS) have been redefined. Mechanical ventilation has evolved from a high tidal volume (V_T), normoxic, and normocapnic approach to a pressure-targeted, lung protective ventilatory strategy (LPVS) aimed at ensuring adequate gas exchange while minimizing transalveolar cycling pressures and volumes.[4] In the February 5, 1998 issue of the *New England Journal of Medicine*, three articles[5–7] and an editorial[8] illustrated the difficulties that clinicians face to demonstrate that LPVS improves outcome in ARDS. In the randomized prospective controlled trial conducted by Amato et al[5] application of a LPVS significantly improved survival as compared with conventional mechanical ventilation. In contrast, the study by Stewart et al[6] failed to reveal any difference in outcome when a LPVS was compared to the conventional approach. The third study by Weg et al[7] challenged the existence of a correlation between the development of pneumothorax or other air leaks and ventilation with high peak inspiratory pressures (PIP). The editorial by Hudson[8] that accompanies these articles questioned whether a LPVS is needed in all patients with ARDS and indicated that plateau pressures (P_{plat}) of 40 to 50 cm H_2O may be acceptable in some patients. Our interpretation of these data differs considerably from that of Hudson. We contend that the results from all three of these trials reveal the beneficial effects of a LPVS and support the use of physiologically targeted, patient-specific ventilatory settings adjusted on the basis of lung mechanics.

In the study by Amato et al[5] 53 patients with ARDS were randomly assigned to conventional mechanical ventilation or to an "open lung approach" LPVS. For 24 patients, conventional ventilator care consisted of volume assist/control ventilation, using square wave flow with peak flows from 50 to 80 L/min, a V_T set at 12 mL/kg, a 0.4 sec inspiratory pause, and a respiratory rate of 10 to 24 breaths/min to maintain arterial carbon dioxide tension(P_{aCO_2}) between 35 and 38 torr. PEEP and F_IO_2 were set to ensure an arterial partial pressure of oxygen (P_{aO_2}) $\geq$ 80 torr with $F_IO_2 \leq 0.6$. In the treatment group (n = 29), ventilation was provided with pressure control or pressure support. A P-V curve of the total respiratory system was constructed to identify the LIP and the upper deflection point (UDP). These points were used to guide the application of mechanical ventilation: PEEP was set 2 cm H_2O above the LIP, and target pressure adjusted to maintain PIP below the UDP. If a LIP was not observed, PEEP was set at 16 cm H_2O, the driving pressure (P_{plat}-PEEP) was limited to 20 cm H_2O, and PIP limited to 40 cm H_2O. F_IO_2 was adjusted to keep the $P_{aO_2} \geq 80$ torr, and the inspiratory time (T_I) was increased if an F_IO_2 greater than 0.5 was required. In addition, whenever airway pressures were allowed to drop to atmospheric pressure, a 35–40 cm H_2O continuous positive airway pressure (CPAP) was applied for 40 seconds to ensure maximal recruitment before ventilation was resumed. Twenty-eight days after enrollment, 18 patients (62%) survived in the treatment group as compared to 7 patients (29%) in the control group. Moreover, the incidence of barotrauma was greater in the control group (42 vs 7%, $p \leq 0.02$), and the weaning rate at day 28 was also higher in the treatment group (66 vs 29%, $p \leq 0.005$).

Stewart et al enrolled 120 patients "at risk" for ARDS in a multicenter, prospective randomized controlled trial in 8 Canadian centers.[6] In the control group (n = 60), V_T was set between 10 and 15 mL/kg with PIP limited to 50 cm H_2O, while V_T was set at 8 mL/kg and PIP was limited to

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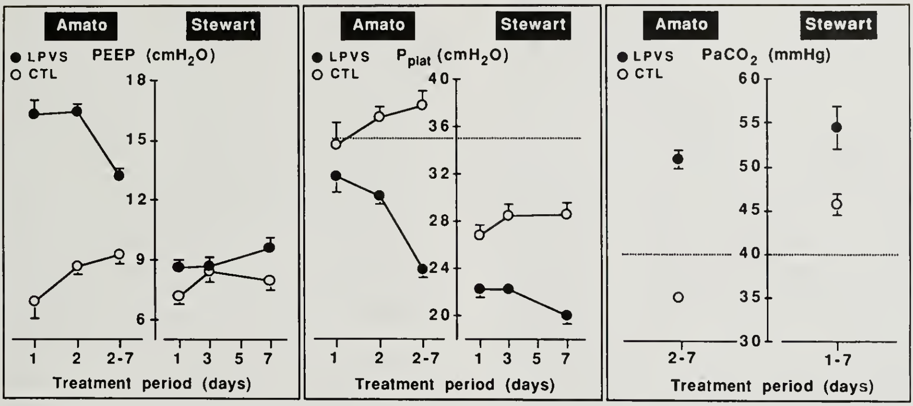

Fig. 1. Evolution of PEEP (left panel), plateau pressures (middle panel) and P_{aCO_2} (right panel) in studies by Amato[1] and Stewart.[2] Data (mean ± SE) are plotted for the first 7 days of each study. LPVS: lung protective ventilatory strategy; CTL: control group. Middle panel: the dashed line represents the maximum plateau pressure recommended by the Americano-European Conference of Consensus. Right panel: the dashed line represents normocapnia. There is a clear separation between the treatment and the control groups in the study by Amato and coworkers. In contrast, a lung protective strategy was used in both groups in Stewart's study.

30 cm H_2O in the treatment group (n = 60). In both groups, mechanical ventilation was provided with volume assist/control ventilation using a decelerating flow pattern, and PEEP was adjusted to maintain arterial saturation oxygen (S_{aO_2}) between 89 and 93% with $F_IO_2 \leq 0.5$. Respiratory mechanics were not assessed in either group. Finally, the target P_{aCO_2} was between 35 and 45 torr, but hypercapnia was allowed in both groups if it resulted from the targeted ventilatory settings. No difference in survival was observed between treatment (50%) and control (53%) groups. A low incidence of barotrauma was reported in the treatment as well as in the control group (10% and 7% respectively). A greater number of patients required dialysis (13 vs 5, $p \leq 0.04$) and received muscle relaxants (23 vs 13, $p \leq 0.05$) in the treatment than in the control group.

Conflicting Results

Since both studies tested the same hypothesis, one must identify the reasons explaining these apparently conflicting results. Figure 1 summarizes the evolution of key ventilatory and gas exchange variables over the first 7 days in both studies. The first and fundamental difference between these studies is the level of PEEP used. In Amato's study,[5] the average level of PEEP (mean ± SE) initially applied in the treatment group was 16.3 ± 0.7 cm H_2O. This was significantly higher than PEEP levels applied in the control group (6.9 ± 0.8 cm H_2O) as well as in Stewart's control (7.2 ± 0.4 cm H_2O) and treatment (8.6 ± 0.4 cm H_2O) groups (Fig. 1, left panel).[6] Such differences in PEEP levels persisted over the first 7 days. In addition, Amato and colleagues used lung recruitment maneuvers (sustained inflation at 35–40 cm H_2O for 30–40 s) whenever airway pressures decreased as a result of disconnections from the ventilator. Differences in lung recruitment may, at least partially, explain the discrepancy between Amato's and Stewart's results.

The second major difference between the two studies was in the inspiratory plateau pressures. In Amato's study,[5] the small difference in P_{plat} at one hour increased over the first 7 days resulting in an unquestionable separation between the treatment and the control groups (23.9 ± 0.7 vs 37.8 ± 1.2 cm H_2O) (Fig. 1, middle panel). In the control group, values for P_{plat} potentially causing overdistention were measured by day 2. In contrast, the P_{plat} observed in both of Stewart's study groups were below 35 cm H_2O throughout the first 7 days,[6] with the maximum P_{plat} only reaching 28.6 ± 0.9 cm H_2O in the control group. V_T and P_{aCO_2} (Fig. 1, right panel) also differed throughout the first 7 days between treatment and control groups to a much greater extent in Amato's study[5] than in Stewart's study.[6] Consequently, it is not surprising that Stewart and colleagues did not observe any difference in outcome between treatment and control groups. In neither group was an overinflation injury possible because of the low plateau pressures applied, and PEEP (which was not set according to the LIP) did not differ between groups. In other words the minimal stretch aspect of a LPVS was applied to *both* groups.

Similarly, application of LPVS in all the patients treated explains the results published by Weg and coworkers.[7]

They observed a 10.6% incidence of pneumothorax or other air leaks in 725 patients with septic ARDS, and did not find any significant correlation between high ventilating pressures or volumes and the development of air leak. It should be emphasized that these conclusions are based on a retrospective analysis of data collected in a study designed to evaluate the effect of surfactant therapy in septic ARDS. The short observation period (5 d), as well as the low sensitivity of the methods used to diagnose pneumothorax or air leaks, seriously limits the significance of the results reported by Weg and co-workers. As indicated by Hudson,[8] pneumothorax in ARDS normally occurs late in the course of the syndrome, when the collagen framework weakens as inflammation develops and remodels the lung's structure. In addition, Weg and co-workers did not list the approach to ventilation nor the P_{plat} used.[7] As a result it is difficult to interpret the significance of an average PIP of 45.9 ± 11.7 cm H_2O. In fact if volume-targeted, square wave flow had been used, the actual plateau pressures may have been between 30 and 35 cm H_2O, particularly considering the increased resistance to gas flow while surfactant aerosol was being delivered to the patient. This easily could be interpreted as a lung protective strategy.

A LPVS Works!

Experimental studies indicate that avoiding overdistention of the lung minimizes the extent of ventilator-induced lung injury,[1] and support the use of PEEP to prevent the development of high stretch lung injury.[2,9–11] Amato's data are consistent with these studies and with previously published clinical investigations[12–14] using a LPVS. In their treatment group, Amato and co-workers addressed both aspects of a lung protective strategy; maximal recruitment and minimal stretch. The use of high PEEP levels together with low V_T prevented both the shear stress injury associated with repetitive opening and closing of the unstable lung[1,15] and the high stretch injury resulting from lung overinflation.[1]

Using this strategy, Amato et al reported an improvement in survival in a group of ARDS patients who appear more severe (no. of extra-pulmonary organ failures = 2.6 ± 1.3) than those studied by Stewart (total no. of organ failures = 1.4 ± 1). In addition, application of a LPVS reduced observed mortality as compared to predicted mortality (38 vs 54%). Maybe key to the improved survival in the LPVS group is the early maximal recruitment of lung, which could minimize consolidation and secondary pulmonary infection. Another explanation could be that application of LPVS limited the development of multiple organ failure, which remains the primary cause of death in ARDS as shown in Stewart's study.[6] Supporting this hypothesis are recently reported experimental studies (reviewed in Ref 16)[16] that suggest that injurious ventilatory strategies can facilitate bacterial translocation from the alveoli into the blood stream,[17] increase pulmonary neutrophil infiltration and adhesion,[18] and stimulate the local production and the systemic dissemination of inflammatory cytokines.[19–21] In addition, Ranieri and co-workers recently observed that inflammatory cytokines decreased in patients with ARDS ventilated with a LPVS, but increased in patients treated with conventional ventilation.[22]

One hopes that other studies will be performed to confirm the results reported by Amato and to define the optimal modalities for implementation of the "open-lung approach." However, it may now be impossible to perform a clinical trial comparing a truly high stretch ventilatory strategy (ie, Amato's control group) to a low stretch LPVS in ARDS. The volumes and pressures used in the control arms of trials by Stewart[6] and Brochard,[23] as well as in the Exosurf trial,[7] clearly indicate that clinicians are unwilling to deliver large V_T and apply high P_{plat}. It is now rare to see ARDS patients ventilated with the large V_Ts (12–15 mL/kg) or airway pressures (70–90 cm H_2O) that were common in the 1970s and 1980s, and data from Hudson's group confirmed that the average V_T used for ARDS in their institution decreased considerably from 1983 to 1995.[24]

In Conclusion

After careful analysis of investigations by Amato, Stewart and Weg,[5–7] we would conclude that all three of these studies support the use of a LPVS in all ARDS patients. Data from Stewart and Weg demonstrate that we have accepted the need to limit peak alveolar pressure to avoid overdistention, and that this is sufficient to decrease mortality as compared to historical control groups. Data from Amato highlight that a LPVS not only includes avoidance of overdistention but also maximal lung recruitment based on assessment of respiratory mechanics. It appears that most of us have been convinced of the detrimental effects of a high peak alveolar pressure. What remains is to convince everyone of the beneficial effects of the use of high PEEP, very early in ARDS, based on the actual respiratory mechanics of the individual patient.

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Critical Care Medicine: The Essentials. John J Marini MD and Arthur P Wheeler MD, Editors. Softcover, illustrated, 640 pages. Baltimore MD: Williams & Wilkins; 1997. $46.95.

Critical Care Medicine: The Essentials by John J Marini MD and Arthur P Wheeler MD, now in its second edition, is a softcover text written entirely by these two specialists in intensive care medicine. The book is organized into three main sections—the first describes techniques and methods in critical care, followed by a section on medical crises, and then a shorter section on surgical crises. Each individual chapter is punctuated by 'key points' that are expanded enough to form a useful summary.

In the authors' words, the content of the book was selected for its interest and practical value and not meant to be comprehensive. Though the intended readership is unstated, it appears to be directed at anyone involved in the clinical care of patients in the intensive care setting. Its stress on basic pathophysiology at the systems level, blended with a clear view toward practical, bedside decision-making, makes this text ideal for the medical student or resident rotating through the 'unit.' However, its clear and thorough treatment of cardiopulmonary physiology would be appreciated by all involved in intensive care, as well as by critical care nurses. Though covering the broad range of subjects encountered in the medical intensive care unit, its evident weight on the physiology of respiratory failure and the principles of mechanical ventilation (ie, separate chapters on positive end-expiratory pressure and weaning from mechanical ventilation) makes these sections extremely valuable for the respiratory therapist. The brief treatment of surgical critical care is acknowledged in the preface and is a reflection of the interests and goals of the authors rather than a weakness.

The book's main strength is the ease with which it moves from physiologic first principles to 'nuts and bolts' medicine. For instance, sections written on the interpretation of pulmonary artery catheter readings, along with useful discussions of calibration, damping, and overwedging, are some of the best. In addition, a new section on ICU utilization and cost control is both practical and thought-provoking. The information is current and fairly weighted, with the most time spent on well-validated standards of diagnosis and treatment, and less in-depth discussions of experimental but promising therapies, such as liquid ventilation, inhaled nitric oxide, and prone positioning in acute respiratory distress syndrome. The absence of specific citations in favor of a 'suggested readings' list for each chapter is in line with the tone of the text. However, many of the recommendations are "drawn heavily from our own clinical experience," and several controversial points are stated as fact; some questionable statements leave the reader wanting to search the specific reference. For instance, the selectivity and effect on glomerular filtration rate of 'renal-dose' dopamine and the ability of flumazenil to reverse the respiratory depressant effects of benzodiazepines are overstated. In addition, rare statements appear to be erroneous, eg, reference to an unachievable "sinus heart rate exceeding (220- age/min)" or the confusing statement that emergency dialysis should be performed in all patients with toxic serum levels of methanol or ethylene glycol.

The readability of this text, unquestionably related to the authors' claim,"every statement has been read aloud," is excellent, and the tables and illustrations are well conceived. There are few if any typographical errors and the index is quite good. The lack of specific citations and comprehensiveness should keep this book from being used as a stand-alone text, but as a companion text for those delivering critical care, it is more than adequate.

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Infectious Diseases of the Respiratory Tract. Michael E Ellis, Editor. Hardcover, illustrated, 605 pages. Cambridge UK: Cambridge University Press; 1998. $200.00.

Infectious Diseases of the Respiratory Tract strives to be "a current, comprehensive, clinically oriented (re)source book on respiratory infections." The book editor acknowledges and emphasizes that physicians from a variety of different backgrounds care for patients with infections of the respiratory tract. Therefore he has attempted to produce a reference book that will cut across the boundaries of traditional disciplines. To this end, the international list of contributors includes pediatricians, internists, pulmonologists, epidemiologists, radiologists, microbiologists, virologists, intensivists, and infectious diseases physicians.

This book is intended for physicians, but a broader audience of health care professionals would find it useful. I found that most chapters were very readable and 'user friendly.' The chapters are organized into three major sections. Part 1 covers diagnostic tests, host defenses, and general principals of antimicrobial therapy. Part 2 includes individual chapters on major respiratory pathogens. Last, the chapters in Part 3, entitled Major Respiratory Syndromes, address general clinical scenarios such as community acquired pneumonia, human immunodeficiency virus (HIV)-associated respiratory infections, and respiratory infections associated with foreign travel. Overall, this organizational scheme works well, allowing the reader to select chapters based either on a specific pathogen or by the general category of clinical setting in which illness occurs.

Several other appealing features of this book warrant mention. The book contains a moderate number of photographs, most of which are informative. Chapters are well referenced, often with over 200 citations each. The chapters regarding new diagnostic methods and tests are very current. I found Chapter 13—Pneumonia Due to Small Bacterial Organisms—especially concise, readable, and informative. The book has an international style that is enjoyable and useful. For example, the discussion of tuberculosis includes epidemiology and treatment issues unique to different regions of the world.

Despite these laudatory characteristics, few books, especially in first edition, are without shortcomings. This book has very few color plates. Many Gram-stains, skin lesions and histopathology slides are shown in black and white. I found only a few minor errors in indexing. Although most of the writing is excellent, there are some spotty lapses in quality and a few sections seem unnecessarily speculative.

Nonetheless, **Infectious Diseases of the Respiratory Tract** is a practical reference that does not merely duplicate the pulmonary infection sections of the major textbooks in infectious diseases or pulmonary medicine. The book is not flashy, but has a distinctive look. The cover is blue with yellow and green graphics. I think this book may find a niche among the many professionals who care for patients with respiratory infections. If so, its relatively minor flaws would ideally be corrected in the next edition.

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Shared Care for Asthma. Mark L Levy, John M Couriel, Roland A Clark, Stephen T Holgate, and Anoop J Chauhan. Softcover, illustrated, 219 pages. Oxford: Isis Medical Media Ltd; 1997. $27.95.

The book is divided into seven chapters. Chapter 1 deals with the scope of asthma and the problems in communicating across the interfaces of the health care spectrum. Chapter 2 is an overview of asthma. As such, it deals with a description of asthma, along with its causes and the financial burdens it places on the individual, the health care system, and society as a whole. Chapter 3 deals with the mechanisms involved in airway inflammation and the cellular biology involved.

Chapter 4 hits upon the specifics of diagnosis (eg, peak expiratory flow), along with the problems both of delayed and of under-diagnosed asthma. Chapter 5 lays down the current goals of asthma management. They are listed: to abolish symptoms, to maintain lung function, to reduce frequency and severity of attacks, and to minimize the incapacity that affects the asthmatic's functioning both at school and at work. Also introduced is the current trend toward using cortico steriods as the first line of defense. Chapter 6 deals with the current care of asthma in the community and in the hospital setting, and how improvements can be made toward a seamless interfacing throughout the health care system. The final chapter presents case studies and examples of referral letters. This chapter deals with specific problems of asthma management, diagnosis, and the essentials necessary for a successful referral to a specialist.

This book was written for primary care health professionals and hospital specialists. However, it should be pointed out that there are no respiratory care practitioners (RCPs) in England. As such, many of the duties ascribed to 'practice nurses' and 'nurse specialists' in the hospitals would fall under the auspices of RCPs here in the United States. Consequently, a large portion of topics relating to seamless care would fall into the RCPs' domain here. I would say that the authors have achieved their overall goal of providing a concise and well-documented need for a seamless approach to the care of the asthmatic patient.

Many of the problems being faced in England are the same ones that we face here: a lack of education among the general practice population pertaining to the current recommendations, both of the National Institutes of Health (NIH)[1] and the British Thoracic Society (BTS),[2] pertaining to treating asthma as an inflammatory disease, with primary treatment consisting of corticosteriods and antileukotriene therapy. Similar problems are apparent in both countries. These include education within the school systems, education of asthmatic families, and education in the hospital setting for recognition and treatment of asthma. Feedback both up and down the health care ladder is also important so that the asthmatic is not misdiagnosed, does not get lost in the shuffle, or have his or her care mismanaged.

The style of the writing is clear and surprisingly concise. There are minor differences due to language, but the few occurrences are easy to interpret. For example, in Chapter 2 on Page 17: "activities such as carrying the wash from the top flat to the drying green" and "taking the push chair up one flight" (referring to uncontrolled asthma and the patients' ability to function normally) pose no problem once the initial confusion has passed. The authors should feel confident that their conclusions are convincing. After reading this text, one becomes sympathetic to the need for increased awareness and cooperative care within the health care system.

The authors cite the BTS guidelines,[2] which mirror the NIH guidelines.[1] For the most part the differences relate to specific tests for asthma. For example, Chapter 4—Diagnosis—states that "variability >15–20% in PEF or FEV_1 is probably due to asthma." The NIH[1] guidelines state the variability as $\geq 12\%$. There are, however some differences that point to variability in medical management. Again, in Chapter 4, on Page 89: "It is generally recommended that the patient should double their prophylatic medications and take their bronchodilators regularly at the onset of a cold until the cold symptoms settle." This does differ from the NIH[1] 'step wise' guidelines.

The book itself is pleasing to the eye and the type makes for easy reading. The tables, charts, and graphs are easy to interpret. I noted no typographical errors. For the topics covered, the references are timely and up to date. The index proved useful for finding subjects once I was done with the individual chapters.

I do feel that those of us who treat the asthmatic patient on a daily basis cannot help but feel a kinship for our brethren from across the Atlantic. Until we can uniformly provide the type of seamless care called for in this text, I fear that we can expect little statistical gain in the battle for decreased morbidity and mortality in asthma care.

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Classic Reprints

STANDARDS OF EFFECTIVE ADMINISTRATION OF INHALATION THERAPY

Second Report by the Committee on Public Health Relations of the New York Academy of Medicine

Recent extension of knowledge concerning the physiology of respiration and the development of improved methods of administering inhalational therapy have made it advisable to review the "Standards of Effective Administration of Inhalational Therapy" formulated by the Committee on Public Health Relations of the New York Academy of Medicine in 1943.[1] It has also seemed appropriate to emphasize again the importance of observing these standards in the everyday practice of inhalational therapy.[2]

Inhalational and Physiologically Directed Therapy

The importance of inhalational therapy in modern medical practice has been shown by its effective use in cardiac failure, coronary artery disease, asthma, atelectasis of the lungs in the newborn, postoperative atelectasis, pneumonia, pulmonary edema, emphysema and cerebral thrombosis, as well as by its value in the treatment of war gas poisoning, respiratory failure due to poisons and other causes, drowning, severe hemorrhage, acute altitude sickness and shock.

The therapeutic use of oxygen is based on the existence of a state of anoxia, that is, lack of oxygen in the tissues. This may be produced by failure of an adequate pressure of oxygen to reach the pulmonary capillaries or by a lowered blood flow which causes a disproportionately large amount of oxygen to be taken out of the capillaries and which results in a diminished oxygen pressure insufficient for normal functioning of the tissues. Oxygen want may develop even with a normal arterial saturation, as in a thrombosis of the coronary, popliteal or cerebral arteries. Treatment in these circumstances makes use of the increased pressure of oxygen physically dissolved in the blood, an accomplishment which not only increases the tension of oxygen through an artery that still may be partly patent but, more significantly, raises the tension in the collateral circulation which feeds the area of the obstructed artery. The most pronounced signs of the physiologic advantages of inhalation of oxygen are a diminution in cyanosis, dyspnea, the pulse rate, restlessness and delerium [*sic*] and a decrease in the volume of pulmonary ventilation.

Although the administration of oxygen is the mainstay of inhalational therapy, other procedures have been developed to improve respiratory function. These include the employment of helium with oxygen, and of oxygen or helium-oxygen mixtures under positive pressure. The usefulness of substituting helium for nitrogen in a respirable gas mixture is due to the lower specific gravity of helium; this property makes it possible to breathe through constricted pulmonary passageways at almost one half the effort required for respiration of air or of pure oxygen. The decreased physical pressure necessary for the inhalation of a helium-oxygen mixture results in a lowering of the elevated negative pressure that occurs within the chest in obstructive dyspnea except in the presence of emphysema. Positive pressure provided during inspiration tends to prevent the excessive negative intrapulmonary pressure from exerting a suction action on the bronchial and pulmonary epithelium and thus is apt to inhibit the collection of excessive mucus within the bronchi and the development of pulmonary edema. Positive pressure within the lungs during expiration precludes severe bronchial constriction and may in some cases retard the flow of blood into the right auricle, allowing the heart to deal temporarily with a smaller

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An abbreviated version first appeared in JAMA, September 2, 1950, Vol 144, pp 25–34. Full version reprinted, with permission of the New York Academy of Medicine.

Prepared by Drs Alvan L Barach, Chairman, Clarence E de la Chapelle, Bettina Garthwaite, Irving M Pallin, Dickinson W Richards Jr, H McLeod Riggins, and Paul M Wood, members, and EHL Corwin PhD, secretary, Subcommittee on Inhalational Therapy of the Committee on Public Health Relations.

[1] Standards of Effective Administration of Inhalational Therapy, Committee on Public Health Relations of the New York Academy of Medicine, JAMA 121:755 (March 6) 1943. Barach AL: Physiologic Therapy in Respiratory Disease, Philadelphia, JB Lippincott Company, 1948.

[2] The results of a survey of the practice of inhalational therapy in hospitals, recently undertaken by the Committee on Public Health Relations of the New York Academy of Medicine, indicated a wide discrepancy between information available concerning methods of administration and the actual conduct of this form of therapy. The final results of this survey will be presented elsewhere. [Survey reprinted, with permission of the New York Academy of Medicine, on pages 749–753 of this issue.]

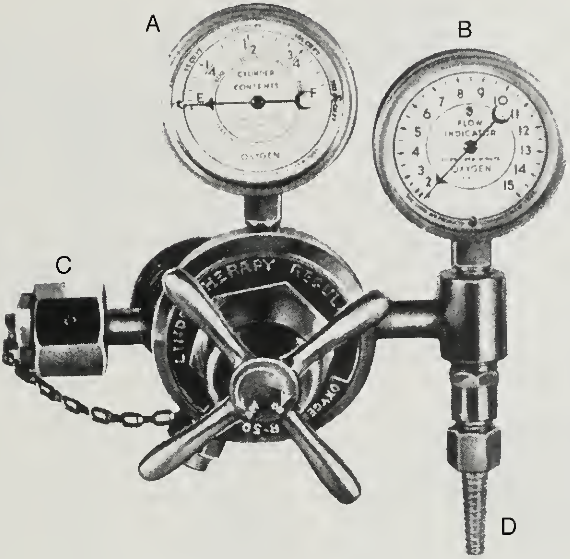

Fig. 1. Oxygen therapy regulator for high pressure cylinders. *A*, pressure and contents of cylinder in cubic feet indicated; *B*, oxygen flow in liters per minute; *C*, attachment to cylinder; and *D*, attachment to rubber tubing.

volume of blood. In addition, positive pressure breathing exerts an opposing pressure on the external capillary wall, tends to prevent edema and counteracts the internal hydrostatic pressure within the capillary.

The local application of epinephrine and phenylephrine hydrochloride by inhalation of nebulized mists brings these agents in contact with the smaller bronchi locally and frequently brings about cessation of bronchial spasm and a decreased swelling of the mucous membrane at a relatively low concentration of the drug in the body. In recent years antibiotic aerosols have been used to combat infections in the respiratory tract; this phase of inhalational therapy is considered at length at the end of this presentation.

In order to regulate inhalational therapy properly, the physician should prescribe the concentration of oxygen and the volume flow per minute, as well as the type of apparatus and, in the newer procedures, the amount and type of positive pressure and the proportion of helium in helium–oxygen mixtures.[2]

Apparatus for the Administration of Oxygen

Cylinders and Regulators. High pressure cylinders with a capacity of at least 220 to 244 cubic feet (6.2 to 6.9 cubic meters) or in the case of half-size cylinders 110 to 122 cubic feet (3.1 to 3.45 cubic meters) should be employed for the administration of oxygen. There is no justification for the use of low pressure tanks, since there is no special "medical" oxygen and only small quantities of oxygen can be furnished in this expensive manner. The oxygen used in medical practice is the same as industrial oxygen.

The pressure-reducing regulator attached to any oxygen cylinder contains two gages; the one proximal to the oxygen tank indicates the amount of gas in the tank and the distal one the rate of flow in liters per minute. Either a variable orifice float gage or a Bourdon tube spring type regulator gage may be employed, provided the gage chosen is made by a reliable standard manufacturer. The gage should be tested from time to time by measuring the rate at which the spirometer bell of a metabolism apparatus is filled at standard pressure and temperature. Before the regulator is attached to an oxygen tank, the oxygen cylinder should first be "cracked," that is, it should be opened slightly until the hiss of escaping gas is heard and then quickly closed. This is done to prevent the initial oxygen stream from blowing dust into the regulator. Oil should not come in contact with the regulator or cylinder valve either from oiling or from the technician's hands.

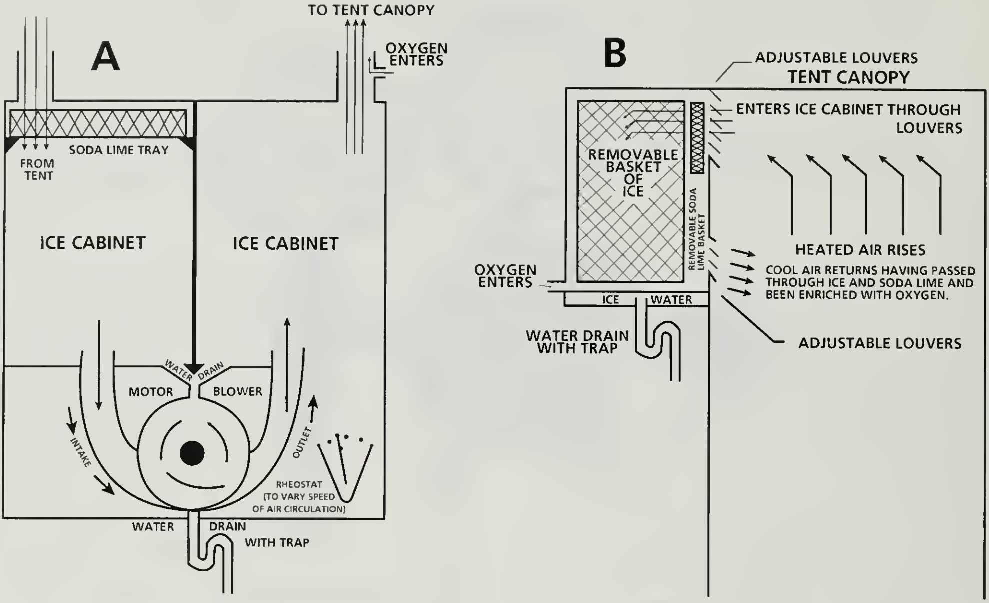

Fig. 2. Circulation diagram of ice-cooled oxygen tents (*A*, motor blower tent; *B*, motorless tent). In the mechanically refrigerated tent a commercial refrigerant (freon®) is used with a compressor unit to accomplish air conditioning, with thermostatic regulation of temperature.

Oxygen Tents. The oxygen tent is a comfortable and effective means of administering 50 to 60 per cent oxygen, provided precautions are taken to prevent undue leakage. The most important error in its use, one which is frequently made, is to allow the motor-driven fan to operate while the tent is opened for the patient to eat or drink or for the physician to examine the patient. It is of considerable importance to turn the motor off before the tent is opened or in ice-cooled tents before ice is added. If this is done, the amount of oxygen lost by diffusion is small and the loss from the refrigerating chamber is eliminated. After the patient has received attention, the tent is closed and the motor turned on again. When this procedure is used, a flow of 15 liters of oxygen a minute for twenty minutes, with a maintenance flow of 10 liters, results in an oxygen concentration within the tent of 50 per cent or higher in the majority of instances.

A maintenance flow of 10 liters of oxygen per minute should be used not merely to keep the concentration at 50 per cent but to wash out the carbon dioxide which would otherwise accumulate in concentrations above 1 per cent, an undesirable amount. When a 60 per cent oxygen concentration is desired, the maintenance flow should be 12 to 14 liters per minute. In practice it is frequently advantageous to prescribe a flow of 12 liters per minute continuously, even for maintenance of an oxygen concentration of 50 per cent, since purging of the tent with 15 liters per minute is then usually not necessary. It is important, however, to test the concentration of a tent with an oxygen analyzer twice daily.

The technician should be equipped to test the carbon dioxide concentration in the tent. When it has been demonstrated that the percentage of carbon dioxide is not above 1 or at most 1.5 per cent under operating conditions, this test need not be performed routinely. The size of the tent does not mean that smaller flows of oxygen can be used. The patient who produces 200 cc. of carbon dioxide a minute must have this diluted with 20,000 cc. of air-oxygen mixture to keep the carbon dioxide concentration at 1 per cent. This is provided by leakage of air in and around the attachments to the bed of the transparent canopy as well as by an inflow of 10 or more liters of oxygen per minute. It is for this reason that soda lime is not needed in any properly constructed tent.

In the modern tent equipped with mechanical air-conditioning the temperature may be set at the desired level by employing the thermostat attached to the tent. It should be borne in mind that the tent does not have to be operated at low temperatures, but should be kept at that temperature

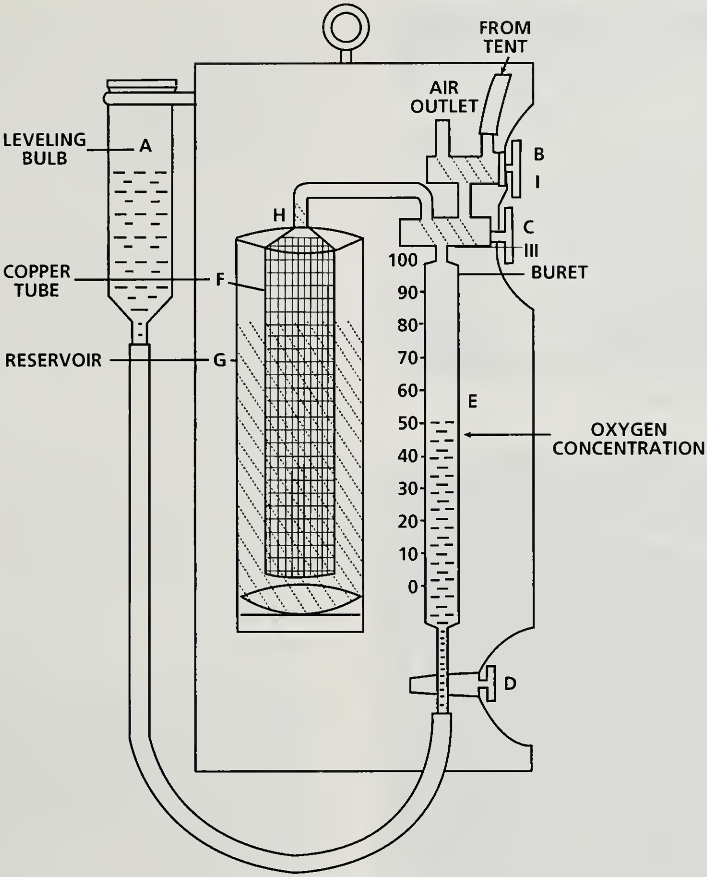

Fig. 3. Oxygen-testing analyzer.

which is comfortable to the patient and preferred by the physician.

For most patients with fever a temperature between 60 and 68 F. is preferred in winter and a slightly higher temperature in summer; for older patients and infants higher temperatures are often desirable. The relative humidity is generally maintained between 40 and 60 per cent. When tents are ventilated by motor blower circulation, which forces the oxygen-air atmosphere over ice or refrigerant (freon®)-filled coils, the humidity will usually be within this range. In certain conditions, such as tracheobronchitis, higher humidities and temperatures than are normally employed may be desirable. Nebulizers or vaporizers may be employed to add water to the atmosphere. The technicians should be instructed to observe and record the temperature in the tent at each visit. If the temperature rises above 70 F., the indication is that there is inadequate cooling and consequently inadequate removal of moisture.

Tents for Infants. The same general principles apply to tents for infants, except that higher temperatures and higher humidities should be prescribed for very young infants. Furthermore, smaller tents may be used. It should be recognized that infants deprived of heat by rapid circulation of cold atmosphere over them may have an abrupt fall in body temperature. A tent with an aperture at the top and with a means of admitting oxygen may be used, provided it is not placed near an open window or door where air

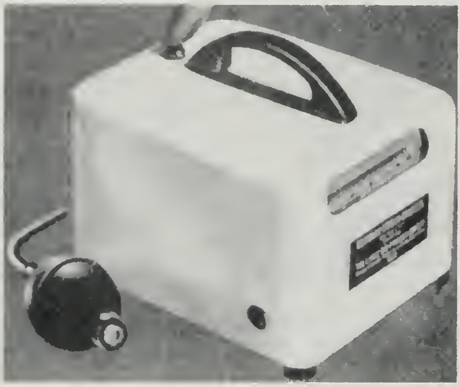

Fig. 4. Electric type oxygen analyzer.

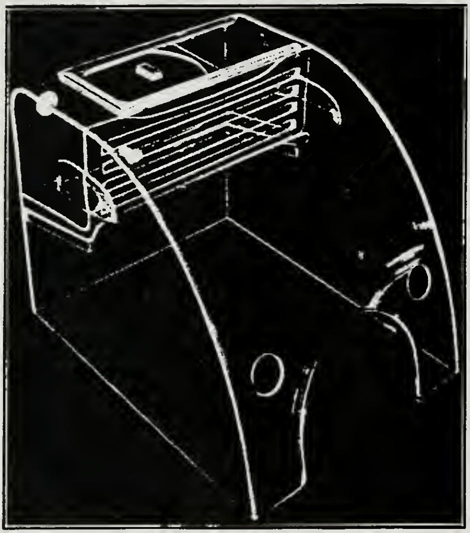

Fig. 5. Infant oxygen hood with built-in ice-cooling compartment.

currents may blow out the accumulated oxygen. It is desirable to test the oxygen concentration in these tents at the level of the infant's nose. Since infants produce little heat, water and carbon dioxide, an open-top tent without an air conditioner may be employed.

An injector meter may be employed for the administration of precise concentrations of oxygen of 40 to 90 per cent in both open box tents and closed head tents. The advantage of the injector is that it provides increased ventilation of the tent with adequate provision for washing out carbon dioxide; for example, a meter setting of 40 per cent oxygen results in an intake of 3 liters per minute of air for each liter per minute of oxygen. Charts are provided which indicate the proper rate of flow required to produce varying oxygen concentrations in both children and adults, as well as the flow required to wash out carbon dioxide in varying circumstances. These head tents may be used with or without ice by the provision of a rack at the back of the head.

Sterilization of the Tent. After the termination of use by each patient the tent should be washed with soap and water inside and outside. It should be finally rinsed with water or rubbed down with 70 per cent alcohol and thoroughly aired. In private practice the use of plastic canopies permits replacement. Ultraviolet lamps have been suggested as sterilizing agents.

Fire Hazards. All tents should be conspicuously labeled "Danger. No flames. No sparks." When a tent is used within a private room, it is desirable to place on the door a sign bearing a similar warning. Oxygen regulators should also be conspicuously stamped "Do not oil." It is suggested that noninflammable transparent material be used in the construction of tent canopies.

Smoking should not be permitted in a room in which an oxygen tent is being used. Electric heating pads or electric call bells should not be permitted within oxygen tents. Visitors should be warned by word of mouth to observe the regulations, as some do not know English or do not read the instructions.

Nasal Administration of Oxygen

Nasal Catheters. There are several effective methods of administering oxygen through the nose: by means of a nasal catheter either in the nasopharynx or in the oropharynx, or by the use of double–bent nasal tubes which just enter the nostrils. The oxygen is first passed through approximately 3 inches (7.6 cm) of water to prevent drying of the mucous membrane. A lubricated nasal catheter, no. 10 or 12 French, is inserted into the nostril for a distance of approximately 3 inches, that is, up to but not touching the posterior wall of the nasopharynx. Six liters of oxygen a minute generally provide 38 per cent oxygen in the inspired air. A single catheter may be used in one nostril at a time if irritation should occur. The terminal 1 inch (2.5 cm.) of the catheter should be perforated with four small holes in order to prevent a single stream of oxygen from impinging on one localized area of the mucous membrane.

If the catheter is passed down into the oropharynx opposite the glottis, a concentration of 42 per cent oxygen in the inspired air may be obtained at a flow of 6 liters per minute. When the catheter is used in the oropharynx, it is

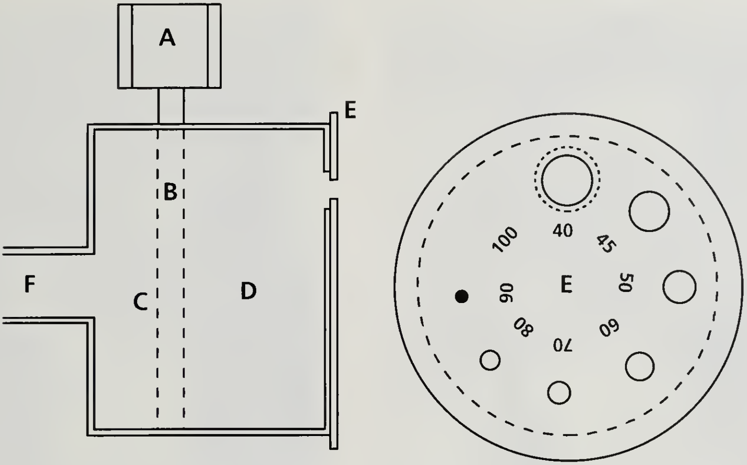

Fig. 6. The injector of the meter mask is attached to the outlet of a standard flow gage by means of a standard nut (*A*). As oxygen enters the mixing chamber (*D*) through the restricted orifice (*C*) a negative pressure is set up in the rear of the mixture chamber. A disk (*E*) containing different-sized openings, each labeled with a percentage number, covers the rear opening of the mixing chamber. By revolving this disk so that any one of its openings is set above the rear opening of the mixing chamber the quantity of air entering the air injector is varied and the percentage of oxygen leaving the mixer outlet (*F*) is thus regulated.

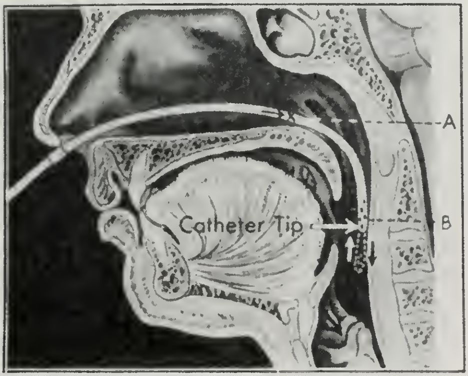

Fig. 7. Nasal catheter: *A*, catheter in nasal pharynx; *B*, catheter in oral pharynx.

important to remember that oxygen may pass into the stomach and distend the abdomen if the catheter is placed lower than the uvula. With the catheter in the pharyngeal position, 7 liters of oxygen per minute may provide concentrations of 45 to 50 per cent oxygen if no sensation of discomfort is produced. When a patient, after insertion of the catheter in the oropharynx, swallows a bolus of air, the inference is that the catheter has been inserted too far; it should be withdrawn until the patient no longer swallows air.

In the use of the nasal catheter the instrument is generally placed in the nasopharynx, as this position is less complicated and safer than the oropharynx behind the uvula. Placement in the latter position admittedly results in a concentration of oxygen in the inspired air approximately 4 per cent higher than is the case with the nasal placement, but caution must be exercised constantly lest the catheter become lodged lower than the uvula; otherwise the stomach may become distended with gas. Furthermore, the administration of 6 to 7 liters per minute will maintain a concentration of at least 38 to 40 per cent oxygen in the average adult patient when the catheter is placed in the nasal pharynx. Mouth breathing lowers to some extent the oxygen percentage in the air inhaled, but this is not significant if breathing takes place through both nose and mouth.

The catheter should be lubricated with water soluble jelly and not with liquid petrolatum or petrolatum, since these are not absorbed by the lungs and may conceivably cause areas of lipoid pneumonitis if blown into the alveoli. It is probable that oil particles formed in this way are so large that they would not reach the alveoli, but this precaution is recommended. Furthermore, the catheter should be changed at six hour intervals to prevent the catheter

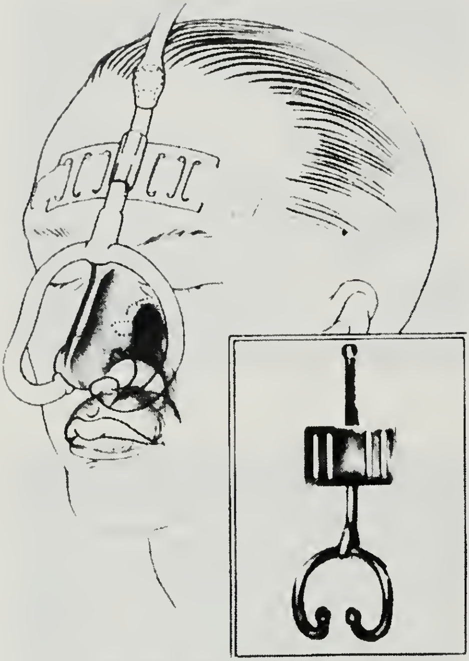

Fig. 8. Bent nasal tubes, metal or rubber.

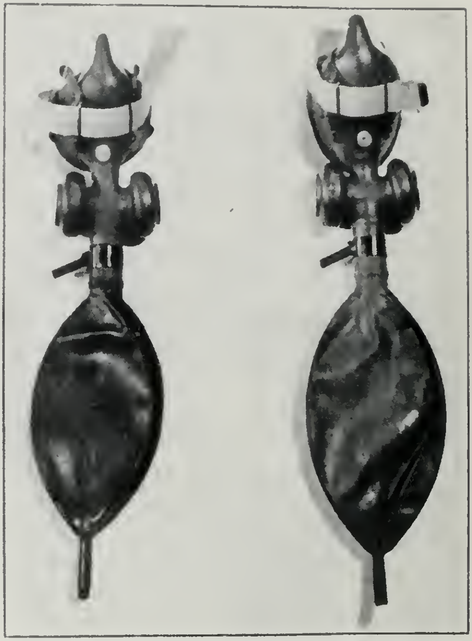

Fig. 9. B-L-B masks with rebreathing bags.

from adhering to the side of the nasal passage after the lubrication is absorbed.

Double-Bent Nasal Tubes. The double-bent nasal tubes of rubber, more comfortable for most patients than the double metal nasal cannula, are serviceable in patients who do not tolerate the nasal catheter in the nasopharynx or the oropharynx. A flow of 7 liters per minute generally results in a concentration of 38 to 40 per cent oxygen.

Masks. Oxygen masks are especially suitable for the intermittent administration of high concentrations of oxygen, from 50 to 100 per cent, and for helium-oxygen mixtures. The nasal catheter is generally more comfortable for long continued use and is just as effective as the oxygen mask when concentrations between 35 and 45 per cent are prescribed. Tents with transparent canopies and air-conditioning cabinets are generally more comfortable for the administration of concentrations between 50 and 60 per cent.

Within recent years it has become apparent that pure oxygen may be irritating to human pulmonary epithelum [*sic*] when administered by a mask continuously for an entire day and irritating to a slight extent in twelve hours. The fact that the mask is removed from time to time for various reasons may be responsible for the reported tolerance of 100 per cent oxygen. Warnings regarding the danger of pulmonary edema from inhalation of these high oxygen concentrations are also based on experiments on animals and human beings kept in airtight chambers continuously. Clinical and experimental evidence has recently indicated that concentrations of oxygen between 50 and 70 per cent have been used for long periods without damage to the lungs; on the basis of this evidence, a large increase in physically dissolved oxygen, provided by 70 per cent oxygen, may be used with great benefit in such conditions as shock, severe hemorrhage, widespread pneumonia and imminent cardiac failure.

There are two masks available, the B-L-B[3] and the Meter[4] mask. The B-L-B mask consists of a close-fitting rubber piece to cover the nose or the nose and mouth; from it is suspended a small bag in which a variable amount of rebreathing takes place. Two sponge rubber disks placed

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[3] The B-L-B mask is named for its designers Boothby, Lovelace, and Bulbulian.

[4] Designed by AL Barach and M Eckmann.

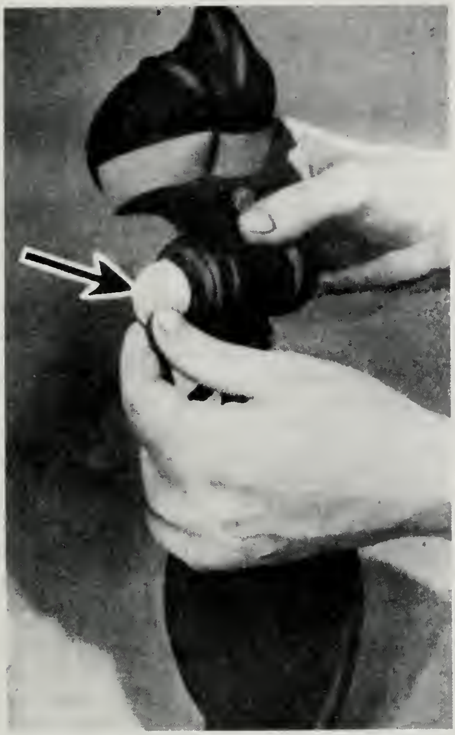

Fig. 10. B-L-B masks with sponge rubber valve (indicated by arrow).

in the center of the mask serve as a combination inspiratory and expiratory valve. During inspiration the resistance in the sponge rubber prevents a free flow of air into the mask. When the rebreathing bag is emptied, air is drawn through the sponge disk. During expiration, the rebreathing bag is first filled with the exhaled air, and the remainder passes through the sponge rubber disk into the outer atmosphere.

During increased ventilation, as in severe dyspnea, the resistance imposed by breathing through the sponge rubber is materially enhanced. This is especially significant during the inspiratory cycle when flows of oxygen under 5 liters a minute are used; in some cases negative pressures within the mask have been recorded in excess of 2 cm. of water. It must also be pointed out that a rate of flow as low as 3 to 4 liters a minute will be accompanied with sufficient rebreathing to produce a carbon dioxide content of 2 per cent or higher in the inspired air; this high percentage of carbon dioxide aggravates the dyspnea of the patient by increasing the volume of breathing about 40 per cent. With the B-L-B mask it is therefore desirable to use a high flow of oxygen, from 7 to 10 liters per minute, in order to eliminate inspiratory resistance and the increased carbon dioxide concentration in the inspired air. For this reason it is impossible to give low oxygen concentrations with this mask without causing excessive rebreathing of carbon dioxide and resistance due to the sucking of air through the sponge rubber disks.[5]

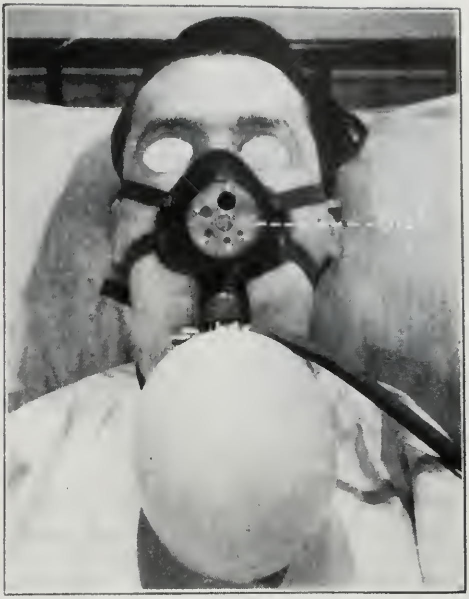

Fig. 11. Meter mask with collecting bag, without rebreathing, and expiratory pressure regulating disk.

In the Meter mask a delicate inspiratory valve is placed between the mask and a large, light latex bag in which no rebreathing takes place; it simply serves as a collecting bag for oxygen. A light rubber flutter expiratory valve is placed in front of the mask for exit of the exhaled air. This mask operates with minimal resistance whether oxygen flow is high or low, provided the reservoir bag is not allowed to collapse completely. An injector is attached to the regulator, which makes possible the administration of oxygen concentrations of 40 to 100 per cent. By the use of apertures of different sizes in the injector, varying amounts of atmospheric air are sucked into the meter because of the negative pressure created by the stream of oxygen passing through it. Calibration of these orifices makes it possible

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[5] It is regrettable that the advertising literature on the B-L-B apparatus continues to list oxygen flows of 3 to 4 liters per minute.

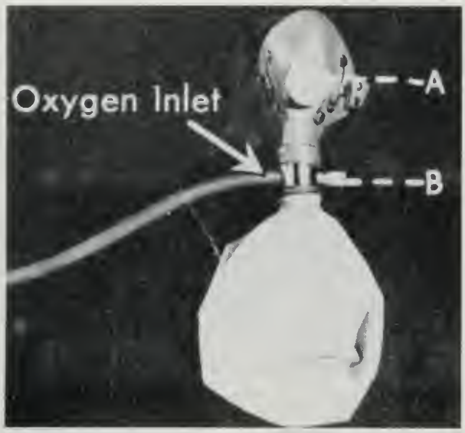

Fig. 12. Meter mask: *A*, expiratory valve, flutter type; *B*, inspiratory valve, disk type.

to provide the desired oxygen concentration immediately with an error of not more than ± 3 per cent. If low rates of flow of oxygen and the exclusion of carbon dioxide from the inspired air are desired, the meter mask is the most suitable. Its use is also indicated in patients with obstructive dyspnea, because in these patients minimal inspiratory resistance is desirable. The rate at which oxygen flows from the regulator may be varied from 4 to 15 liters per minute, depending on the concentration desired and the volume of flow required to prevent the collecting bag from collapsing. The employment of less than 4 liters a minute is seldom indicated except for young children, for whom lower rates of flow may be adequate.

Although the masks are comfortable for some patients, it must be recognized that their continuous use becomes objectionable to many others. When discomfort prevents the continuous administration of oxygen by mask, a shift should be made to the oxygen tent, when feasible, or to nasal catheters, a hood or a face tent.

After use, the mask should be scrubbed thoroughly with soap and water and should be immersed or washed in a 70 per cent solution of alcohol.

Pressure Breathing. Pressure breathing apparatus is of three general types:

1. Expiratory positive pressure breathing devices. These are simple appliances in which the patient exhales against a resistance, increasing the intrapulmonary pressure during expiration.

2. Continuous positive pressure breathing equipment. These types of apparatus provide continuous positive pressure in both inspiration and expiration.

In both these types the flow of air is continuous, and the patient breathes spontaneously.

3. Apparatus for artificial respiration. The simplest and most useful of these devices are those designed for intermittent positive pressure breathing, in which air or oxygen enters the lungs under positive pressure in inspiration; pressure is then automatically released, and expiration occurs as a passive act. Such apparatus is used in patients with depressed or failing respiration, as in coma or poisoning. Other apparatus for artificial respiration, of the "suck and blow" type, is also available.

The Oxygen Mask Metered for Positive Pressure. The Meter mask may be equipped with a metal disk which surrounds the expiratory flutter valve and contains on its external surface five orifices of different diameters. When the largest orifice is employed, expiration proceeds naturally without pressure. When the disk is turned to the smaller orifices, the patient exhales under a positive pressure of 1, 2, 3, or 4 cm. of water, depending on the size of the orifice and the volume of breathing. More accurate control of pressure is obtained when expiration is conducted through a water bottle calibrated in centimeters of water.

The use of positive pressure during expiration is specifically indicated for the treatment of acute pulmonary edema occurring in various conditions, such as pneumonia, left ventricular failure, some cases of shock and irritant gas poisoning. In oxygen therapy for patients with pulmonary edema it is customary to begin with pressure of 5 cm. of water and gradually lower it to 2 and then 1 cm. From 40 to 60 per cent oxygen is employed. The injector attached to the regulator is turned to the oxygen percentage desired, and the flow from the regulator is adjusted at that rate; this arrangement prevents the collecting bag from collapsing at the end of inspiration. It is desirable to have the injector one third full of water so that the stream of oxygen may pick up moisture as it passes into the mask. Distensible rubber bags which will provide some positive pressure in inspiration also are now being developed.

The relative humidity of pure oxygen passing at a flow of 8 to 10 liters a minute through the injector partially filled with water is approximately 20 per cent at 70 F. The inspired oxygen is additionally moistened by the inner surfaces of the mask, which are wet with the saturated water vapor resulting from expiration, so that the ultimate relative humidity of the inspired oxygen is approximately 45 per cent. If a still higher relative humidity is desired during inhalation of 100 per cent oxygen, the injector is removed and a water bottle attached to the regulator, so that the stream of oxygen will pass upward through at least 3 inches of water before entering the mask. However, air is usually employed in concentrations of 30 to 40 per cent, which contributes the moisture prevailing in the atmosphere.

Positive pressure is employed also to prevent or control the oozing that takes place from the tracheobronchial tree following tracheotomy. When this is used, the tracheotomy tube is prolonged so that expiration proceeds through an expiratory valve into a water bottle at pressures which generally begin at 4 to 5 cm. of water and are gradually lowered during a period of twelve hours to 1 to 2 cm. of water.

Positive pressure respiration should be administered cautiously in shock, in which the venous return to the heart is retarded, but increased intrapulmonary pressure of 2 to 4 cm. of water may be considered safe if plasma or blood is given concomitantly: When peripheral circulatory failure is suspected, the blood pressure should be followed at fifteen minute intervals and the intrapulmonary pressure reduced or discontinued if a fall greater than 10 mm. of mercury takes place in the systolic pressure after the application of breathing under positive pressure.

Continuous Pressure Breathing. Pressure breathing in inspiration and expiration is used for the treatment of asthma, for obstructive lesions in the larynx and trachea and for pulmonary congestion and edema. An effective device for pressure breathing in inspiration and expiration makes use of weights on two rubber bags into which 40 to 50 per cent oxygen is admitted from an injector; or, if desired, helium-oxygen mixtures may be used. A mask is employed in this apparatus, which is simpler although less comfortable for prolonged use than the positive pressure hood formerly employed.

Inspiratory pressure may be built up swiftly by setting a specially constructed injector meter at a concentration of 40 per cent oxygen. This injector actually delivers 38 per cent oxygen, at a flow of 15 liters per minute, with a total gas flow of 65 liters per minute of air plus oxygen. With lower rates of flow, the building up of inspiratory positive pressure is less rapid.

Although pressures of 4 to 6 cm. of water are generally used for the treatment of obstructive dyspnea and pulmonary edema, higher pressures have been employed for brief periods in severe obstructive dyspnea and for resuscitation. When higher pressures are used, the effect on circulation is more pronounced and may lead to a decrease in cardiac output, especially in patients with impaired circulation. In shock, positive pressure, when employed, should be used with the precautions that have been mentioned.

In obstructive dyspnea the greatest degree of relief is secured if an 80 per cent helium-20 per cent oxygen mixture is employed with pressure breathing. The injector is then not used, but a continuous flow of 7 to 9 liters per minute of the helium-oxygen mixture is provided.

The pressure breathing device described herein is also equipped with an emergency inspiratory valve, placed on the inspiratory side of the rubber tubing. Air may be introduced at any time through this valve, if the inspiratory collecting bag should for any reason collapse through the development of a leak. The patient is thus protected against breathing under a negative pressure.

Artificial Respiration. In respiratory failure, with depressed or inadequate respiratory stimulus, artificial respiration may be required. Such conditions include: poisoning with barbiturates, morphine, carbon monoxide and some of the more toxic alcohols; drowning, certain types of coma, poliomyelitis with respiratory paralysis and electrocution.

In any form of artificial respiration, with unconscious or stuporous subjects, special attention must always be given to clearing the airways. Mucous and foreign matter must be removed by suction or other means, the tongue kept well forward and the position of head and neck maintained in extension, with the chin somewhat elevated. In the presence of bronchospasm or respiratory tract edema, inhalation of bronchodilator drugs in the course of the artificial respiration may be useful. The even expansion of the chest during inspiration should be maintained at all times.

Manual methods of artificial respiration, such as the prone pressure (Schaefer), technic, do not provide adequate ventilation and are difficult or impossible to use for prolonged periods.[6] The Eve rocking procedure is more effective but again difficult to apply in most clinical situations. An anesthesia bag and mask can be used for short periods, the operator compressing the oxygen-filled bag by hand to provide inspired air, and allowing expiration to occur passively. In this procedure there is usually enough leakage around the mask and enough flushing out of the bag with oxygen to prevent accumulation of carbon dioxide in the bag to any serious extent.

Special hand-operated intermittent positive pressure respirators are available. In these, air is forced into the chest by a hand bellows until a certain maximum pressure is reached (usually 10 to 15 mm. of mercury); then a valve is tripped, and the patient exhales passively into the outside air. The bellows is filled again from the air or from an oxygen tank, and the process is repeated. These forms of apparatus are useful for short periods.

For continued artificial respiration some type of automatic respirator is necessary. One of the practical difficulties with all such apparatus is to provide a tight–fitting mouthpiece or mask. Face masks with cushion rubber or inflatable rubber sides are the most widely used, but these

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[6] An effective method (JH Emerson) consists of raising and lowering the patient's hips while he is in the prone position.

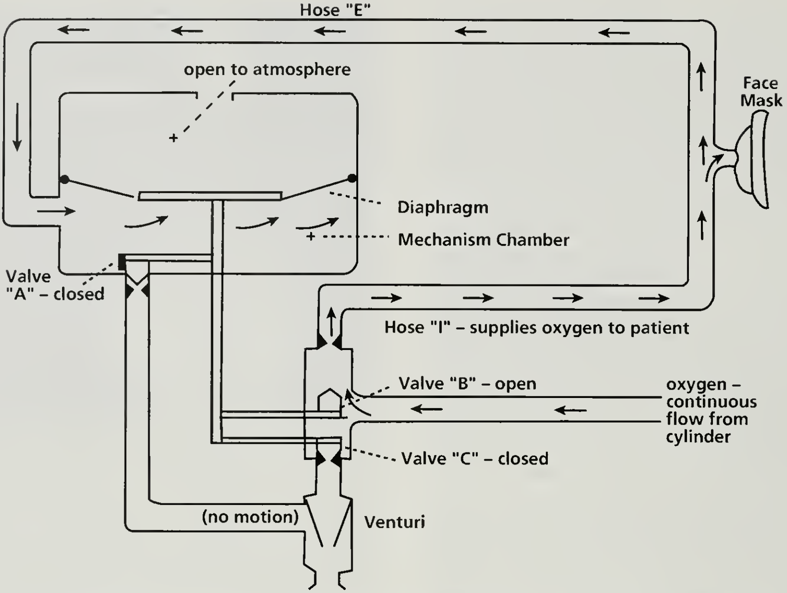

Fig. 13. Emerson resuscitator, inhalation phase. Hose "I" carries only pure oxygen from the oxygen cylinder to the patient and never carries exhaled gases. This feature is covered by U. S. patent no. 2,268,172 and Canadian patent no. 405,705.

must be strapped on tightly and constantly watched for displacement and leaks. In profound respiratory depression requiring hours or even days of continuous artificial respiration, intratracheal intubation by an anesthesiologist may be at times the best procedure.

The simplest artificial respirators are the intermittent positive pressure types. The essential features are an oxygen tank, a demand valve and a second, or cycling, valve. Air flows into the mask until a certain pressure is reached; then the inflow is shut off and expiration proceeds until the pressure in the mask is reduced to a certain low pressure (usually zero); then the cycling valve opens, oxygen flows from the demand valve and inspiration begins again. The pneumatic balance resuscitator is an effective form of this cycling apparatus, as are some of the other resuscitators. It should be emphasized that this apparatus will cycle also with the patient's own respiration, following recovery of his spontaneous inspiration and expiration; its operation thus differs from that of the Drinker type respirator, with which respiration is imposed.

Since intermittent positive pressure respiration provides a mean positive pressure over the respiratory cycle, it may be effective in reducing or preventing pulmonary edema in unconscious subjects. An intermittent positive pressure system has been used for as long as three days continuously, in a case of barbiturate poisoning, with maintenance of cardiopulmonary function. At the cycling pressures provided by this apparatus, there is in most cases no significant retarding effect on the venous return of blood to the heart.

The positive and negative pressure (suck and blow) respirators are also effective and safe to use with unconscious subjects. There is no convincing evidence that these forms of apparatus have deleterious effects either on the lungs or on the circulation. In fact, the mean average pressure, which is near zero, actually produces less impairment of venous return in patients with circulatory insufficiency. It should be noted that a rapid tripping indicates that oxygen is not reaching the alveoli because of some obstruction and that a slow tripping with coincident chest expansion indicates a good gaseous exchange. Slow tripping without adequate chest expansion may be due to a slow leak, usually at the point of application.

Some use has been made of respirators, especially the intermittent positive pressure types, on conscious subjects. In some instances, as when respiratory muscular exhaustion is severe or when pulmonary edema is present with relatively little dyspnea, the intermittent positive pressure respirator has been helpful in relieving symptoms. Generally, however, conscious subjects in need of respiratory

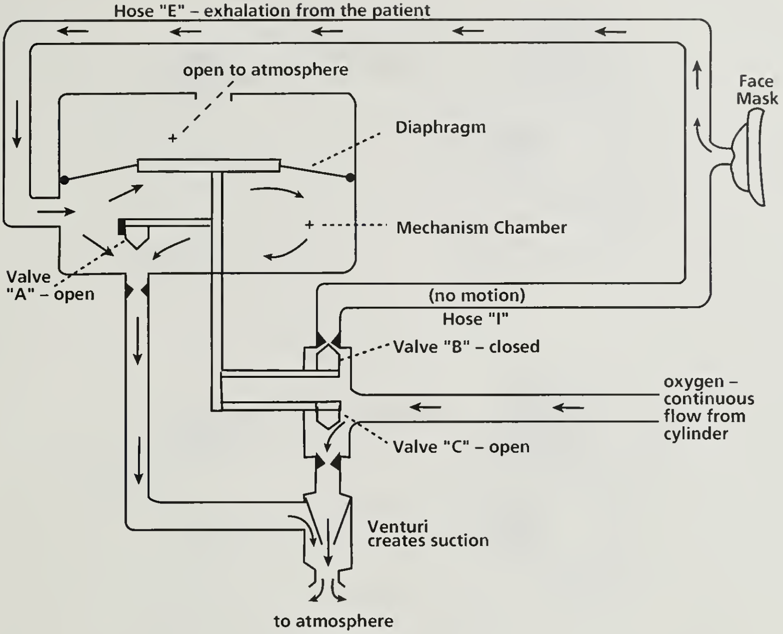

Fig. 14. Emerson resuscitator, exhalation phase.

aid are also dyspneic, requiring quick inhalation of air during the early phase of inspiration. Since most respirators cannot provide a rapid immediate volume of inflow, the patient inhales against a resistance in early inspiration with a sensation of increased dyspnea or suffocation. Intermittent positive pressure respirators have been devised with an inflow capacity of extremely large volume (100 liters per minute) during early inspiration, but these are not commercially available at present.

The Pressure Equalizing Chamber. The pressure equalizing chamber provides an adequate exchange of gases within the lung by a swift variation in air density, accomplished by a change in pressure within the chamber of 120 mm. of mercury twenty–five times a minute. As air is first admitted into the head end of the chamber and then passes beneath a collar that surrounds the patient's neck, the pressure exerted on the outer surface of the wall of the chest is reduced to a degree that equals exactly the resistance in the respiratory passageway. Ventilation of the lung then proceeds without any change in lung volume.

This chamber has been used to immobilize the lungs in the treatment of chronic pulmonary tuberculosis; in recent studies it has been found that patients with obstructive dyspnea, such as those with intractable bronchial asthma and pulmonary emphysema, are promptly relieved of dyspnea during residence in the chamber. A varying higher pressure in the head end of the apparatus is required to overcome the increased resistance in the bronchial tubes. Additional pressure, greater than that required to overcome bronchial resistance, accomplishes pressure breathing at the start of inspiration. The patient may breathe without difficulty in a chamber of this type, since the differential pressure between the head and body ends of the chamber is generally not more than 3 or 4 mm. of mercury. Artificial respiration may therefore be conducted in an apparatus of this sort with or without positive pressure.

The Respirator. It should be recognized that maintenance of artificial respiration in a respirator is, in effect, achieved by positive pressure breathing. A negative pressure within the respirator of 12 mm. of mercury, which causes the lungs to expand, is equivalent to an increase in positive pressure on the face of 12 mm. of mercury. Since the pressure falls to that of the atmosphere in each instance, a mean average pressure, depending on the pressure curve, of 6 mm. of mercury is generally present. In other words, respiration conducted by the respirator, al-

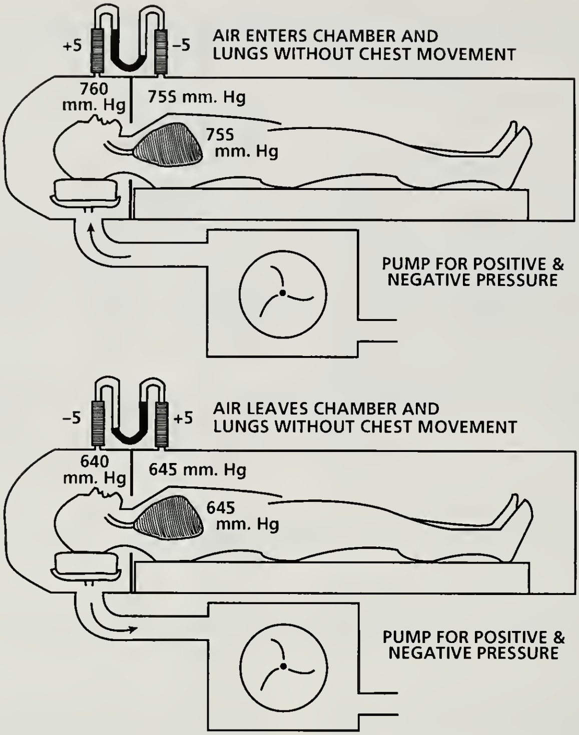
+5
-5
AIR ENTERS CHAMBER AND LUNGS WITHOUT CHEST MOVEMENT
760 mm. Hg
755 mm. Hg
755 mm. Hg
PUMP FOR POSITIVE & NEGATIVE PRESSURE
-5
+5
AIR LEAVES CHAMBER AND LUNGS WITHOUT CHEST MOVEMENT
640 mm. Hg
645 mm. Hg
645 mm. Hg
PUMP FOR POSITIVE & NEGATIVE PRESSURE

Fig. 15. Pressure equalizing chamber provides lung ventilation without lung movement when pressures on outer and inner surfaces of chest wall are made equal by counterbalancing the resistance in the respiratory passageway.

though it is induced by intermittent negative pressure within the chamber, is a form of intermittent pressure breathing in which inspiration is accomplished by a rise in pressure of 12 mm. of mercury and expiration by return of pressure to that of the atmosphere.

In most forms of intermittent pressure breathing hyperventilation is apt to take place. An increase in oxygen saturation resulting from loss of carbon dioxide does not contribute to the overcoming of anoxia, since a loss in the pressure of carbon dioxide in the tissues is in most instances approximately equivalent to a loss of oxygen pressure. With slight increases in pulmonary ventilation, the oxygen tension gained in this way may not be offset by the mild alkalosis engendered. In the administration of intermittent positive pressure, therefore, precautions should be observed to prevent excessive loss of carbon dioxide by overbreathing. In contrast, the use of continuous pressure breathing is not accompanied with hyperventilation. The effect of the pressure used in continuous pressure breathing appears to be equivalent to the mean pressure of intermittent pressure breathings. For purposes of resuscitation, intermittent pressure breathing of some form is naturally indicated, and not continuous pressure respiration.

Administration of Helium-Oxygen Mixtures

A mixture of 80 per cent helium with 20 per cent oxygen, which is employed in the treatment of asthma, obstructive lesions in the respiratory tract and pulmonary atelectasis in the newborn may be administered in the positive pressure hood apparatus already described, but this requires skilled technical service and is generally too cumbersome for ordinary use. The usual method of administering helium and oxygen is by the employment of a comfortable mask without rebreathing. Since inhalation of the helium–oxygen mixture is designed to relieve obstruc-

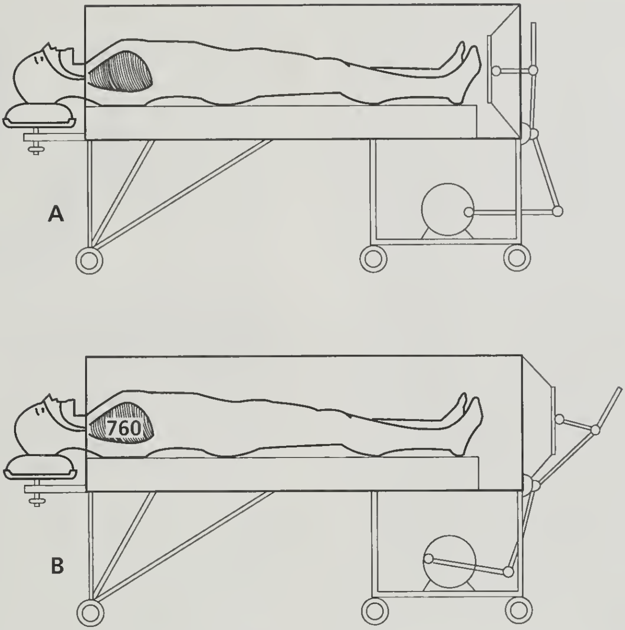

Fig. 16. Artificial respirator. At the end of exhalation (*A*) the pressure both at the upper airway and surrounding the body is 760 mm of mercury. Therefore no gradient exists between the pressure around the body and that at the nose and mouth. When a partial vacuum is created in the respirator (*B*) the pressure surrounding the body is 748 mm of mercury and the pressure inside the patient's lungs is 760 mm of mercury, greater than the pressure surrounding his thorax. The effect of this gradient is to cause inhalation as the thoracic cage is pushed out by pressure from within.

tive dyspnea, the slightest accumulation of carbon dioxide is a pronounced disadvantage, because an increase in the volume of breathing will correspondingly increase the effect of obstruction. Thus, if a patient is breathing at a pulmonary ventilation of 8 liters per minute, with a certain degree of respiratory obstruction, and the volume of breathing rises to 12 liters a minute as a result of the presence of 2.5 per cent carbon dioxide in the atmosphere, the pathologic effects of obstructive dyspnea are also increased 50 per cent. It is therefore desirable to use the meter mask, with the valve above the collecting bag, which prevents any rebreathing in the rubber bag. In most cases the mask may be used at atmospheric pressure with a flow of 7 to 8 liters as indicated on the ordinary oxygen regulator. It must be remembered that the flow indicated on the regulator should be multiplied by 1.7 in order to get the true flow of helium-oxygen mixture. In other words, the restricted orifice of the regulator is itself a demonstration of the higher rate of flow at a given pressure of a mixture of 80 per cent helium and 20 per cent oxygen.

More effective relief of obstructive dyspnea is provided by inhalation of helium–oxygen mixture under positive pressure during both inspiration and expiration; this relief may also be obtained by the device previously described that produces pressure as a result of a weight on both the inspiratory and expiratory collecting bags. The periodic inhalation of helium and oxygen under continuous pressure of 3 to 6 cm. of water is employed for the treatment of asthma, obstructive lesions in the respiratory tract and pulmonary edema. In the treatment of pulmonary edema it is desirable to reduce the pressure gradually, for example, about 1 cm. of water pressure at hourly intervals until the patient is breathing at atmospheric pressure.

Administration of 5 to 10 Per Cent Carbon Dioxide in Oxygen

The administration of 5 to 10 per cent carbon dioxide in oxygen is useful in carbon monoxide poisoning. Carbon dioxide–oxygen inhalation has also been employed in massive collapse of the lungs, in order to stretch the bronchi and perhaps loosen a tenacious plug of mucus, and for short periods after operations to expand the lungs and bronchi, but the evidence in favor of its value in the prevention and treatment of atelectasis has been questioned by many investigators. These carbon dioxide–oxygen mixtures should not, however, be left in a lung in or near the atelectatic state, since all these gases may be quickly absorbed and atelectasis thus rendered complete. In other words, atmospheric air (containing 79 per cent nitrogen) must be vigorously inhaled at the end of any treatment, in order to fill the alveoli with nonabsorbable nitrogen.

Carbon dioxide in oxygen is particularly useful in intractable hiccup. For this purpose a tank of 90 per cent oxygen and 10 per cent carbon dioxide may be employed with either a B-L-B or a meter mask for periods of two or three minutes or until the patient just loses consciousness. In some cases 15 per cent carbon dioxide for one and one–half to a maximum of two minutes produces better results. It must be borne in mind that prolonged administration of carbon dioxide will bring about toxic symptoms, such as headache, nausea, and (when concentrations above 15 per cent are employed too long) convulsions. It should also be noted that carbon dioxide is a powerful cardiac whip; it produces hypertension and excessive diaphoresis due to its action as a central vasoconstrictor and a peripheral vasodilator.

Many cases of intractable hiccup that are resistant to 5 per cent carbon dioxide inhalation may be successfully treated with concentrations of 10 to 15 per cent carbon dioxide when employed up to the point of loss of consciousness. The cessation of hiccup appears related to a central effect on the brain rather than to sustained pulmonary ventilation. In cases of depressed respiration due to morphine or barbiturate poisoning, carbon monoxide is not indicated, since the carbon dioxide content of the blood is already high. This also applies to atelectasis of the lungs of the newborn.

Administration of Drugs by Inhalation

Nebulization of Bronchodilator and Antibiotic Aerosols

The purpose of inhaling nebulized solutions is to deposit on the respiratory passageway and in the alveoli small droplets of substances suspended in air. The size of the particles in therapeutic aerosols exercises a critical effect on the site of deposition and absorption from the respiratory tract. Particles of small size, 0.3 to 0.8 micron in radius, pass readily through the tracheobronchial tree into the alveoli, where varying proportions from 60 to 70 per cent, are absorbed, depending on the complex nature of the substance. Particles of relatively large size, more than 10 microns in radius are mostly precipitated on the pharynx, larynx, trachea and larger bronchi.

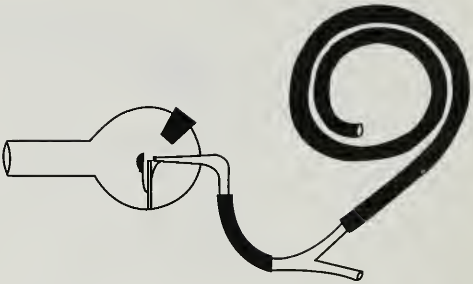

Fig. 17. The nebulizer may be used with the Y tube connected to an oxygen cylinder or to a pump. It is also conveniently employed by the patient with a hand bulb without a Y tube.

The determination of the optimal particle mass for therapeutic administration depends on the location where deposition is desired and on the therapeutic substance employed. Thus, in the treatment of bronchospasm it is desirable to use a nebulin of bronchodilator solution of relatively small particle size (1 to 3 microns in radius) in order to obtain both local application to the smaller bronchi and absorption from the alveoli into the blood stream. Similarly, it is desirable to avoid the use of a vasoconstricting nebulin of large particle size in order to prevent useless deposition of drug and irritation of the larynx and trachea.

In the treatment of bronchopulmonary infections with penicillin and other antibiotic aerosols, deposition of the drug on the surface of the bronchial mucous membrane as well as absorption from the alveoli into the blood stream are accomplished by inhalation of mists of relatively small particle size, 1 to 3 microns in radius. Although maximum alveolar absorption takes place with smaller particles, 0.4 to 0.8 micron in radius, the time required for administration of mists of such small particle size is considerably prolonged with the nebulizers now in use. When treatment of nasopharyngeal and sinus infections is intended, use of an antibiotic aerosol of larger particle size appears to be desirable in order to obtain greater deposition of the drug in the nasopharynx and, with use of intermittent negative pressure, in the sinus cavities.

Treatment with nebulized bronchodilator solutions in bronchial asthma and pulmonary emphysema is conveniently carried out by the hand bulb nebulizer with 1:100 epinephrine solution, 2.25 per cent racemic epinephrine or arterenol (isopropyl epinephrine). Continuous nebulization of epinephrine and related substances, as well as chemotherapeutic substances such as the sulfonamide drugs and glucosulfone sodium (promin®), may be maintained with air from a pressure pump and with oxygen from high pressure cylinders. The sulfonamide aerosols have been largely superseded by the newer antibiotic drugs, especially penicillin and streptomycin, because of their greater clinical effectiveness. Streptomycin aerosol has been used in the treatment of bronchial and laryngeal tuberculosis, in conjunction with parenteral administration of streptomycin.

The introduction of penicillin into the nasal accessory sinuses is accomplished by the development of intermittent negative pressure in the nasal passages during the nebulization of penicillin aerosol in concentrated solutions, such as 50,000 to 100,000 units per cubic centimeter.

Inhalation of micronized or powdered penicillin and powdered streptomycin, recently introduced as a simple method of topical application, requires further study to appraise its value, but it appears at present to be less effective and more wasteful of drug than penicillin or streptomycin aerosol in the treatment of bronchopulmonary infections.

Methods of Administering Penicillin Aerosol

The administration of penicillin aerosol calls for an appropriate nebulizer and a source of air or oxygen under pressure. For the cooperative patient oral inhalation is employed. A glass Y tube is inserted in the rubber tubing between the nebulizer and the oxygen regulator; the finger is placed over the open end to close it during inspiration and removed during expiration. A mouthpiece attachment and a rebreathing bag may be used if it is desired that the patient reinhale some of the penicillin from the expired air; this arrangement also prevents spilling of the penicillin solution into the mouth. When a mask is employed a demand valve may be connected to the nebulizer, by which penicillin aerosol is produced only during the inspiratory cycle through a slight drop in pressure actuating the demand valve. A hood or tent is employed for simultaneous administration of penicillin and oxygen in dyspneic patients. The dosage of drug commonly used is 50,000 to 200,000 units of penicillin dissolved in 1 to 2 cc. of saline solution or distilled water.

An important detail of technic is to use one or two rinses in the nebulizer after the penicillin solution has been nebulized, since without rinses 40 per cent of the drug remains in the nebulizer in concentrated form. The rinse solution may be distilled water, saline solution, vasoconstricting and bronchodilating solutions, such as 1 per cent phenylephrine hydrochloride, 1 per cent racemic epinephrine or 1 per cent ephedrine, or benzalkonium chloride 1:1,000.

Apparatus for Use of Antibiotic Aerosols in Sinusitis

The nebulizer used for administration of penicillin aerosol in the treatment of infectious sinusitis should preferably be one which produces particles of relatively large size, such as a nebulizer of the Vaponefrin® type from which the baffle has been removed and in which the diameter of the jet has been lengthened. A greater deposition of penicillin particles in the nasal passages and perhaps a larger concentration in the accessory sinus cavities may then be provided by the use of alternating positive and negative pressure. It should be emphasized, however, that for the treatment of bronchiectasis an aerosol with a relatively small particle size, which is produced by the standard Vaponefrin®, DeVilbiss, or S.P.S. nebulizer, is preferable. The baffleless nebulizer, used only for sinus and nasal infections, has the advantage of swift production of a coarse mist with the hand bulb, 1 cc. being nebulized in five minutes.

A single nose piece with a small glass trap attached to the nebulizer to contain secretions is generally employed for the treatment of sinusitis. The patient breathes through the open mouth as the mist is nebulized into the nasal passages by air or by oxygen. An oxygen flow of 5 to 8 liters per minute is employed. Negative pressure may be produced by a Venturi tube connected to the nebulizer or, in the simpler apparatus, by a hand bulb. When one uses the Venturi tube, one must close the open end with the thumb; this forces oxygen or air to pass through the nebulizer and form the aerosol. When the thumb is removed from the open end of the tube and the patient swallows, a negative pressure is created in the nasal passages and in the antrums. When suction in the nose is felt by the patient, the thumb is promptly placed again on the Venturi tube, to direct the aerosol into the nasal passage.

The pressure required may be generated by high pressure oxygen cylinders, by a motor pump, an automobile foot pump, a hand operated fire pump or a hand bulb. The dose of penicillin which is frequently used is 50,000 to 200,000 units dissolved in 1 to 2 cc. of saline solution, or 1 per cent phenylephrine hydrochloride solution or boiled water. The Venturi tube and the nebulizer should be washed every day or two; the nose pieces should be washed after each treatment.

The Hand Bulb Method of Producing Negative Pressure. The nebulizer may be used with a hand bulb instead of the Venturi tube to produce negative pressure. Positive pressure produced by compression of the rubber bulb forms the mist, and negative pressure is developed when the bulb expands. The patient inserts the single glass nose piece into the nostril, compresses the hand bulb to produce the aerosol, then closes the other nostril with the finger, and swallows as the bulb expands, producing a negative or suction effect in the nose. When the experience of negative pressure is noted, the bulb is again compressed, producing an aerosol of penicillin in the nasal passages. The advantage of the bulb technic of producing negative pressure lies not only in its simplicity but also in the fact that the penicillin mist enters the nasal passages during the latter part of the phase of negative pressure, as the bulb expands. Since 1 cc. of solution may be nebulized by the hand bulb in five to ten minutes when the large jet, baffleless nebulizer is employed, this apparatus lends itself to home treatment, without the use of oxygen or a motor-driven pump. More effort is naturally required for the hand bulb method than with the use of a source of pressure, such as a cylinder of oxygen or an air pump, or hand or foot pumps. However, in each instance a negative pressure of 50 to 60 mm. of mercury may be attained in the nasal passages and transmitted to the accessory sinuses.

Clinical Illustrations of Need for Instruction

The lack of adequate teaching of inhalational therapy was recently manifested in a clinic on inhalational and physiologic therapy of respiratory disease. Four problems in treatment were presented for which physiologically directed therapy was indicated.

A statement of each case history was presented, with a request for a correct answer, to a group of forty physicians interested in diseases of the chest. Only four of them had answers that would aid the patients.

Case 1. A patient with pulmonary emphysema was short of breath as a result of upper respiratory infection. She was placed in an oxygen tent at a flow of 7 liters per minute, with the canopy carefully tucked in on all sides, and with a temperature and humidity within the normal range. A concentration of 60 per cent oxygen was obtained one hour later. However, the patient revealed increasing shortness of breath which was relieved promptly after the tent was removed. The previously existing dyspnea returned to the same degree present before treatment with oxygen. What was the cause of the increased dyspnea in 60 per cent oxygen?

Case 2. A patient with bronchial asthma was treated in a B-L-B mask at a flow of 4 liters per minute to provide a concentration of 40 per cent oxygen, according to the literature that came with the mask apparatus. Within fifteen minutes there was a pronounced increase in the dyspnea of the patient which was relieved after the mask was removed. What was wrong in the handling of this patient?

Case 3. A patient with hypertensive vascular disease and coronary arteriosclerosis had acute widespread pulmonary edema at night. After treatment with a Meter mask, providing an expiratory positive pressure of 5 cm. of water, the lungs were clear at the end of one hour. The mask was removed, but within thirty minutes there was a return of pulmonary edema. What form of treatment was then indicated?

Case 4. A patient manifested acute widespread edema of a lung after six days of continuous inhalation of 95 to 100 per cent oxygen in a B-L-B mask. The pulse rate was 150; the respiratory rate was 70. An expiratory positive pressure mask, with a pressure on expiration of 5 cm., was used and the oxygen concentration was lowered to 60 per cent. A decided increase in cyanosis took place. What should the subsequent program of treatment have been?

Clinical situations of this type are common, and, unfortunately, the inability to prescribe proper treatment is revealed not only among general practitioners but among specialists in diseases of the chest.

In case 1 increased dyspnea was due to a carbon dioxide concentration of 2.5 per cent, which resulted from the low rate of flow of oxygen (7 liters per minute) and an inadequate washing out of carbon dioxide. The patient who eliminates 250 cc. of carbon dioxide per breath must have this diluted in 2,500 cc. of air plus oxygen in order to lower the concentration to 1 per cent. A flow of not less than 10 liters per minute, maintaining an oxygen concentration of 50 per cent, must be used in order to bring about a dilution of carbon dioxide and thus prevent increased pulmonary ventilation and aggravation of dyspnea. To maintain a concentration of 60 per cent oxygen requires a flow of 12 to 14 liters per minute.

In case 2 a flow of 4 liters per minute in the B–L–B mask was insufficient to wash out carbon dioxide; the concentration of carbon dioxide in the mask was 2.5 per cent. In addition, the collapse of the bag during inspiration made it necessary for the patient to suck air through the sponge rubber disks, which required increased inspiratory effort. The negative pressure within the mask when the sponge rubber disks are new may be from 1 to 1.5 cm .of water, but when they are clogged with dust the resistance is even higher. The patient with bronchial asthma should have a flow in a B–L–B mask of not less than 7 liters per minute in order to wash out the major part of the carbon dioxide and to prevent collapse of the bag during inspiration. (In the injector type meter mask the mixture of oxygen and air takes place at the regulator as a result of the pressure of oxygen itself in the injector.)

The patient with pulmonary edema in heart disease (case 3) was treated again with a Meter mask providing an expiratory positive pressure of 5 cm. of water; when the moisture had cleared, pressure was gradually lowered from 5 to 4 cm., 4 to 3, 3 to 2 and 2 to 1, i.e., a lowering of 1 cm at half hour intervals. In these circumstances the heart was offered a gradually increased volume of blood, so that left ventricular failure was not indicated by sudden entrance of a large amount of blood.

In case 4 treatment was continued with 60 per cent oxygen, since this concentration is not irritating to the lungs. Despite the temporarily increased cyanosis, the patient was decidedly improved; at the end of thirty–six hours the pulmonary edema had subsided. The pressure was gradually lowered, and the patient ultimately recovered.

These cases are cited in order to emphasize the lack of knowledge on the part of physicians concerning the functioning of the apparatus that is commonly employed, as well as an incomplete understanding of the pathologic physiology of the conditions themselves.

Need for Trained Personnel

The advantages of theoretic knowledge of the physiology and pathology of respiratory disorders are not transmitted to the patient unless the technics are skillfully administered. Because of the complexity and diversity of modern apparatus, technicians must be properly trained and supervised. In New York City the Board of Health conducts examinations for licensure of technicians in inhalational therapy. Although at present licensure applies solely to those in the business of supplying inhalational therapy services and proprietary hospitals, it provides an opportunity for extension to hospital personnel. Hospitals have not generally considered it feasible to supply trained technicians for the administration of inhalational therapy; it is usually relegated to a changing intern staff or to nurses and orderlies who as often as not have not had proper instruction.

The fact that few medical schools and hospitals provide instruction in inhalational therapy is another factor responsible for a lack of competent supervision of this type of treatment of conditions due to impaired respiratory function. Frequently the trained technician is more familiar with the procedures than is the physician, a situation which in all probability will continue until adequate teaching of inhalational therapy is undertaken by medical schools and hospitals.

Still another factor appears to be the unwillingness of physicians interested in respiratory physiology or in diseases of the chest to assume the directorship of departments of inhalational therapy in the absence of full time trained technical assistants. Physicians who refuse such assignments would appear to be abundantly justified, since they themselves would be called on either to carry out in person time-consuming procedures or else to take responsibility for improper practice by poorly trained hospital personnel.

In some hospitals the anesthesiologist has been placed in charge of the therapeutic use of gases and pressures because of his familiarity with the inhalation of anesthetic agents. Unfortunately, clinical problems at times arise in disturbances of respiratory function in which he is not qualified as a consultant. To establish him in the role of glorified technician in charge of equipment and technic is of advantage neither to him nor to the hospital. If hospitals were required to provide trained inhalational therapy technicians, the physician specializing in respiratory disease might be interested in heading such a department, conducting studies on those clinical entities characterized by impaired respiratory function and providing the hospital clinic with consultative services, when desired; such services might prove to be of value to those of his colleagues less well informed concerning the physiologic and technical problems involved.

Summary

The purpose of inhalational therapy may be broadly described as the attempt to restore normal function to the respiratory system. Impairment of respiratory function ultimately manifests itself in a lack of oxygen in the tissues. At times this may be counteracted by simple inhalation of an oxygen-enriched atmosphere. In recent years, however, the recognition of more complex pathophysiologic changes in the organs of breathing has stimulated the development of various means of controlling pressure as well as the therapeutic use of gases.

Alleviation of anoxia is frequently of crucial importance in such conditions as cardiac failure, coronary artery disease, asthma, pulmonary emphysema, atelectasis of the lungs, pneumonia, pulmonary edema, and cerebral thrombosis. A proper understanding of the technics of modern procedures in inhalational therapy is essential if the value of this type of physiologically directed therapy is actually to be brought to the bedside. An attempt has been made herein to formulate the methods now in use in order to promote a more effective employment of inhalational therapy.

Although no emergency is more critical in clinical medicine than an interruption in the lifeline of oxygen, the failure to teach inhalational therapy in medical schools is almost universal.

The lack of skilled technicians in many hospitals is responsible for inexpert management of the methods of treatment, which are generally relegated to a changing intern staff, nurses, or orderlies.

Physicians interested in respiratory physiology or in diseases of the chest would seem to be the most suitable as heads of departments of inhalational therapy in hospitals because of the complexity of the problems in internal medicine for which consultative services are needed. However, without specially qualified technical assistants the director would find himself carrying out procedures of a burdensome and time-consuming nature, or, equally unfortunately, delegating serious responsibility to unskilled personnel.

Registration of technicians and technician supervisors who have been qualified by written and oral examinations, as already established in New York City by the Board of Health, constitutes the beginning of a program whereby hospitals may acquire an expert inhalational therapy service. This type of service is of crucial importance in the management of the many clinical entities characterized by impairment of respiratory function.

ADDITIONAL REFERENCE

Andrews, A. H., Jr. Manual of Oxygen Therapy Techniques, Chicago, Year Book Publishers, Inc., 1943.

THE SURVEY OF THE STATUS OF INHALATIONAL THERAPY IN THE HOSPITALS OF NEW YORK CITY

Report of a Subcommittee of the Committee on Public Health Relations of the New York Academy of Medicine

Since 1931 the Committee on Public Health Relations of New York Academy of Medicine has maintained an active interest in inhalational therapy. At that time the Committee sponsored an exhibit and drew up standards for oxygen equipment following an inquiry into the prevailing practices. A second study, dealing with effective administration of oxygen, was made in 1936, and another in 1943, when the "Standards for Effective Administration of Inhalational Therapy" were prepared by a special subcommittee and published in the Journal of the American Medical Association. The 1943 Subcommittee assisted in drafting a local law passed by the Council of the City of New York, placing purveyors of oxygen therapy service under the supervision of the Department of Health.

Again the need to review the current status of this mode of therapy has been brought to the attention of the Committee. In January of 1949 a questionnaire was sent to 167 hospitals and 99 nursing homes in the five boroughs of New York City and Westchester County. Eight major phases of the question were included in the inquiry. These were: (1) Personnel in charge of inhalational therapy, (2) equipment, (3) administrative practices, (4) service by private purveyors, (5) payment, (6) records, (7) extent of use of inhalational therapy during 1948 and (8) aerosol therapy.

Returns were received from 50 per cent of the hospitals and from six nursing homes. Examination of the replies confirmed the current reports that the knowledge now available regarding this mode of therapy is not being fully applied in present administrative practices; that some institutions apparently have no one on their staffs sufficiently familiar with it; and therefore in many institutions practices persist which are hazardous to the patients. In the replies received from hospitals maintaining their own equipment, discrepancies were frequent between the information reported in the questionnaire and facts known to members of the Subcommittee. Some replies were so fragmentary that it has been necessary to supplement the returns from the questionnaire with information derived from other sources. It is true that the questionnaire asked for a great deal of information; it seemed reasonable that a hospital staff member charged with the supervision of this service should be in possession of the answers to these questions if he were really aware of the resources and hazards presented by inhalational therapy. Lack of interest on the part of the managing officers was another factor which reduced the effectiveness of the survey, for some hospitals which are known to maintain high standards did not reply.

The administration of drugs is carefully checked in reputable hospitals, yet in some institutions oxygen is given without adequate supervision of the particular needs of the individual patient. This may lead at times to serious consequences; for example, an accumulation of carbon dioxide within an oxygen tent or mask may stimulate the rate of respiration and in an asthmatic patient may aggravate dyspnea.

This report is divided into three parts:

I. Information Derived from the Questionnaire
II. Information Derived from other Sources
III. Conclusions and Recommendations.

PART I. Information Derived from the Questionnaire

A detailed analysis of the reports received cannot be made, since of the 83 hospitals whose replies were tabulated, none submitted complete information. The data here presented are therefore but fractional.

Supervision

In 49 hospitals oxygen equipment was supplied by outside sources. In 10 of these the private purveyor had sole supervision of inhalational therapy. In 40 the purveyor was responsible for the actual administration of inhalational

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therapy with varying degrees of assistance from the hospitals. Although the regulations of the New York City Department of Health defined standard practices which must be adhered to by purveyors "engaged in the business of supplying inhalational therapy service," the Subcommittee seriously questions the desirability of delegating to purveyors the complete responsibility for this form of therapy without medical supervision.

Of 11 different groups listed in the returns as responsible for the supervision of inhalational therapy, the largest classification is that of anesthesiologists. Familiarity with the physiology of respiration and with the use of gases has been the basis for this delegation of responsibility to them. Interns and residents are not trained in the majority of hospitals or medical schools to assume responsibility for the administration of inhalational therapy, yet in 8 hospitals in the New York area, according to this survey, interns and residents have sole responsibility for administration. In a few, they are even charged with supervision; multiple responsibility, reported in twelve hospitals, tends to encourage carelessness in therapeutic procedures. One hospital reported that five different groups of people had charge of the service.

Training for Personnel

Fifty-three hospitals reported that their staff members receive training in inhalational therapy; the amount of training was not usually specified. One well-known hospital stated that student nurses were afforded one lecture per year, and it seems probable that this is the general picture. About half of the hospitals maintaining their own equipment train the technicians who operate it. Nine hospitals reported that the training offered is equal to that required for licensure by the city.

Equipment

According to the survey, 33 of the 83 hospitals own their own equipment; 40 rent it, and 10 combine owned and rented apparatus. It has been estimated that in an active general hospital the number of inhalational therapy units should approximate 10 per cent of the number of beds. Forty-six percent of the participating hospitals fell within this standard, if the number of regulators (oxygen flow meters or Bourdon type gauges) be accepted as a measure of equipment ready for use. A piece of equipment is not considered complete unless it is accompanied by a regulator so that it may be attached to a tank of gas or to a piping system. Of the 33 hospitals maintaining their own equipment, 19 reported a number of regulators equal to 90 per cent of their pieces of equipment; the average for all the hospitals reporting was 55 per cent.

Approximately half of the institutions reported some aerosol equipment on hand.

Operating Practices

In regard to checks for motor failure, 25 hospitals supplied no information; 20 replied that some check was made, ranging from "daily" to "as necessary," or "as need is indicated," 2 definitely reported that no check was made, and 16 stated that the motor was checked after each use. One hospital reported that motors were examined "every 2 hours," and another reported checks every 60 days. Information as to temperature control was not indicated by 27 hospitals; 31 gave no information concerning proper ice water drainage, and replies concerning tests for obstruction in the ice cabinet were fragmentary. Twenty-four hospitals offered no information as to whether a mask or hood in use was checked for leakage.

Cleansing of Tents

According to the regulations of the Department of Health, purveyors are required to wash the tent cabinet and canopy with soap and water inside and out, and then rub the canopy down with 70 per cent alcohol or dip it in 1:1000 bichloride of mercury solution or in some other effective chemical before the next use. Although 49 hospitals reported that soap and water were used for the cleansing of tents, only 30 reported that tents were cleansed after each use, and 63 did not answer a question as to the sterilization of infant tents with a chemical. One hospital reported that canopies were washed only if the patient had a contagious disease, and three were wont to wash the canopy "when necessary."

Rate of Oxygen Flow

Although it has been repeatly emphasized that a flow rate of oxygen into a tent cannot safely be less than 10 liters per minute in order to dilute to a reasonable degree the amount of carbon dioxide emitted by a patient of average size, only 39 hospitals reported using a flow rate of 10 liters or more. Of the ten municipal hospitals that replied to the questionnaire, seven stated that they employed a flow rate of less than 10 liters a minute.

The Subcommittee was informed that the rates of oxygen flow are sometimes reduced by unauthorized persons in the interests of economy; tents have been observed in operation at flows of 3 to 4 liters. Failure to appreciate the importance of the correct concentration of oxygen within a tent during treatment is apparently a frequent occurrence; a large number of hospitals did not report whether the concentration was routinely determined.

Economy of operation is admittedly an important consideration. Since shutting off the motor blower while nursing care is given to the patient conserves a considerable amount of oxygen that would otherwise be wasted, the question was raised as to how often the motor is thus stopped. It was found that 75 per cent of the hospitals observe this precaution.

Record Forms

Only 10 hospitals reported the use of special medical forms to record the inhalational therapy procedures. Considerable variation was found in the amount of oxygen used in those hospitals from which this information was available for the preceding year; the reported application of inhalational therapy in a year ranged from 3 hours per bed in one general hospital to 30.4 *twenty-four hour days* per bed in another.

Payment for Service

Eighteen different systems of payment by patients for inhalational therapy were found in the various hospitals, including those with purveyors. These ranged from the all-inclusive rate used in 7 hospitals to direct payments made by the patient to the purveyor. The most common plan, used in 21 hospitals, is to base charges on the use of equipment plus a charge for the gas used.

Responsibility for Arrangements for Private Service

The payment of rebates to physicians by individual purveyors was presented as one of the serious problems in connection with the maintenance of professional standards for this service in some hospitals. The Subcommittee is of the opinion that a contract between a hospital and a single purveyor eliminates this unethical practice to an appreciable degree. Only 4 hospitals reported that individual physicians were allowed to make arrangements with private purveyors.

PART II. Information Derived from Sources Other than the Questionnaire

An inadequacy in the management of inhalational therapy equipment has been observed even in some of our best hospitals; in one instance, examination showed that only 15 per cent of the equipment on hand was in usable condition, and only 50 percent could be rendered usable.

In some hospitals that maintain good equipment its effectiveness is nullified by improper use. The supervisory head of the inhalational therapy service is in many instances far removed from the actual administration, which may be carried out by inadequately trained orderlies or by nurses unfamiliar with the correct operation of equipment. Too often, a physician orders an oxygen tent and leaves no instruction as to the details of its application; the same physician would not simply order digitalis and leave the dose to the discretion of a nurse, technician or an untrained employee.

Inhalational therapy equipment may be in excellent condition, but it may not give satisfactory results either because those in charge do not understand its functioning or because it has been inadvertently disarranged by nurses or visitors. Purveyors have observed that the cause most frequently found for the failure of an oxygen tent is that the electric cord has been disconnected from the wall socket.

One type of oxygen mask in common use contains a flutter valve in the nosepiece, permitting release of expired air into the room. It has been observed time and time again that this valve had been taped down tightly because "it fluttered and appeared to be a defect in the mask." In some instances bags have even been removed from this type of mask because they did not fill completely.

The function of these bags is to collect oxygen as it flows from the tank while the patient is exhaling and to hold it for inhalation. Unless there were some method of storage, large amounts of oxygen would be wasted. The proper adjustment of this type mask requires that the bag be only partially filled during exhalation. If it were fully distended, the pressure would force oxygen to leak from the edges of the mask. With such an arrangement for storage of oxygen it is possible to use a lower rate of flow. When, for lack of understanding, the bag is cut off, the patient simply breathes room atmosphere. Private purveyors report that the oxygen flow in tents and masks is often reduced as a measure of economy.

In tents cooled with water (wet) ice, attempts are sometimes made to preserve the ice by wrapping it in paper. As a result, bits of paper may plug the drain, allowing water to accumulate and thus obstruct the flow of gas to the patient. Although all manufacturers of wet ice tents state plainly that large chunks of ice must be used in the cooling compartment, shaved or cracked ice has been used; ice in this form freezes into a solid mass, which obstructs the flow of gas to the patient. On the other hand, it has been suggested that dry ice (solid carbon dioxide) be used in a wet ice compartment to overcome the drainage problem of wet ice; there was no realization that lethal quantities of carbon dioxide could thus be inhaled by the patient. It has been observed at times that the ice compartment was being used as a storage icebox for the patient's home-provided ginger ale or fried chicken.

PART III. Conclusions and Recommendations

The Committee on Public Health Relations of the New York Academy of Medicine has conducted surveys for many years. Invariably the response to questionnaires has been most generous. The return of only 50 per cent of the questionnaires in this study and the fact that none was complete seem to indicate that hospitals do not integrate this form of therapy into their organization and that they therefore do not feel too willing to report on it.

In a large proportion of instances physicians who should be competent to supervise the administration of inhalational therapy in hospitals are prone to delegate this responsibility to technicians. Nurses, who are in most hospitals directly charged with the administration of the major part of the inhalational therapy and who are, moreover, often called upon to administer medical gases to patients at home, have little or no training to fit them for the task.

The Subcommittee on Inhalational Therapy is of the opinion that the prevalence of practices which not only deprive the patient of benefits that he might receive, but may actually endanger his life are the result of the lack of systematic instruction regarding the assets and liabilities inherent in this mode of treatment. Training programs for interns, residents and nurses are generally inadequate. Purveyors offer technical training courses to the hospitals in which they supply equipment, but they have stated that they are rarely called upon for this special service.

On the basis of the information obtained in this survey, the Subcommittee offers the following recommendations:

1. Medical schools should give instruction in inhalational therapy to their students and should offer special courses for interns and practicing physicians.
2. A program of instruction should be arranged for nurses, technicians and others who may be charged with the administration of medical gases. It is suggested that the New York City Department of Health be urged to sponsor a suitable course for technicians and nurses, with certificates for those successfully completing the work. A satisfactory course might consist of six 3-hour lectures and demonstrations, twice weekly for three weeks, and it could well be repeated quarterly for the convenience of the hospital personnel.
3. Hospitals should set up within their organizational pattern provision for medical supervision of inhalational therapy.
4. As final supervisory responsibility for therapy lies with the physicians on the hospital staff, the medical board of each hospital should decide for the particular hospital the advantages of maintaining its own equipment as compared with those offered by contract with a purveyor.
5. Hospitals should make use of standard forms to check on the condition of the available equipment and its use.
6. The regulations now enforced by the New York City Department of Health which apply to purveyors and proprietary hospitals should be reviewed, and the scope of their application should be enlarged to include voluntary and municipal hospitals on an equal basis.
7. Copies of this report should be sent to the administrators and the medical boards of all hospitals in the New York area and subsequently submitted for publication in a local medical journal.
8. A spot check survey should be undertaken within the next two years to appraise the effect of the educational effort made by the Academy through the exhibit and lectures in the Symposium presented December 5–10, 1949, and through this survey, as well as the revision of the Standards of Effective Administration of Inhalational Therapy to be published in the Journal of the American Medical Association.

Respectfully submitted,
Oswald R Jones MD Chairman
Russell L Cecil MD
Chesmore Eastlake Jr MD
George Goodstein Esq
Irving M Pallin MD
EHL Corwin PhD Secretary

Approved by the Committee on Public Health Relations May 15, 1950.

Suggested Check List For Inhalational Therapy Apparatus

Checks and Intervals to Ensure Proper Function

REGULATORS
- Leaks—after each use
- Accuracy—monthly

CATHETERS
- Patency—four times daily
- Rotting—daily
- Sterilization—before each insertion

HUMIDIFIERS
- Seal tight—daily
- Holes plugged—daily
- Odor—daily
- Sterilization—after each use

TENTS, all types
- Canopies
  - Tears—daily
  - Sterilization—after each use
- Chassis
  - Water drain patent (water ice tent)—with each ice refill
  - Drip pan empty (mechanical refrigeration)—daily
  - Ice compartment seal tight—with each ice refill
  - Leak around blower shaft—weekly
  - Oil motors—see manufacturer's instructions
  - Replace filters—see manufacturer's instructions

MASKS, all types
- Meter Mask OEM
  - Flutter valve soft and not torn—daily
  - Inspiratory and accessory inspiratory discs functioning—daily
  - Bag leak—daily
  - Connector right side up—daily
  - Meter face tight—daily
  - Venturie hole aligned—after each use
  - Suction plug in—daily
  - Sterilize—after each use
- B. L. B.*
  - Bag Leak—daily
  - Suction plug in—daily
  - Sterilize—after each use
  - Sponge discs not clogged with dirt or water—daily
  - Bag drain plug in—daily

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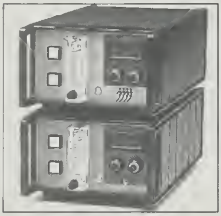
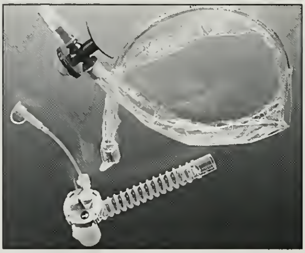
* The B-L-B mask is named for its designers Boothby, Lovelace, and Bulbulian.

New Products & Services



O_2 AND CO_2 GAS ANALYZERS. VacuMed announces it has received FDA clearance to market O_2 and CO_2 gas analyzers. According to the company, both analyzers include a permanent "Nafion" gas dryer, side-stream sample pump, digital display, and analog signal output for recording or computer interfacing. VacuMed says the O_2 analyzer uses a research-grade permanent paramagnetic sensor that has 0.1% O_2 accuracy over the range of 0 to 100% O_2 and that the CO_2 analyzer uses a fast response infrared sensor that has 0.1% CO_2 accuracy over the range of 0 to 10% CO_2. The company says the CO_2 analyzer offers a choice of continuous or end-tidal display and that both outputs are available on rear panel BNC connectors. For more information from VacuMed, circle number 150 on the reader service card in this issue or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/

TRANSFILL SYSTEM. Andonian Cryogenics Inc offers the HP-40 Skid-Mounted Transfill System. Company literature states that this system converts liquid oxygen to a high pressure gas for filling high pressure medical cylinders; the cylinders are connected, evacuated and automatically filled. According to Andonian, the system can fill more than 55 'E' cylinders per hour using low-cost liquid oxygen, and a combination of aluminum, steel, and fiber-wrap cylinders can be refilled at different pressure settings up to 3,600 PSI. The complete system includes 60 or 140 liter liquid oxygen storage container, liquid oxygen pump, manifold, oxygen analyzer, and vacuum pump. For more information from Andonian Cryogenics, circle number 151 on the reader service card in this issue or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/

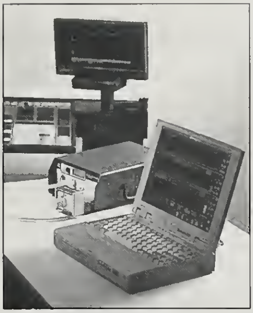


PULMONARY HYGIENE SYSTEM. Mallinckrodt Inc offers the Hi-Care™ System. Corporate literature describes this system as a closed suction and pulmonary hygiene system with detachable atraumatic catheter. According to Mallinckrodt, the sleeved suction catheter reduces the risk of cross contamination for patients and staff and the detachable feature allows bronchoscopy and mucus sampling without disconnecting ventilatory support. The company says the system's rotating valve may be positioned so that the suction catheter is isolated from the patient's airway when not in use and that the distal portion of the suction catheter features an ultra-soft, rounded tip with multiple eyes to reduce the risk of trauma or blockage. For more information from Mallinckrodt, circle number 152 on the reader service card in this issue or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/

ISE REAGENTS. ALKO Diagnostic Corporation recently developed reagents for use on the ISE modules of the Olympus AU600™, AU800™, AU1000™, and AU5200™. According to the company, all of their consumables serve as functional equivalents to those distributed by the original equipment manufacturer, and they offer correlation data upon request. ALKO says these reagents are designed to provide quantitative determinations of Na, K, and Cl concentrations on the previously listed devices and that all reagents are packaged to fit conveniently into the analyzer. For more information from ALKO Diagnostic Corporation, circle number 153 on the reader service card in this issue or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/

PULSE OXIMETER. BCI International offers the Autocorr™ Pulse Oximeter with SAC™ (serial autocorrelation) Data Acquisition Technology. Corporate literature says the device uses refined hardware and patented software to extract data in a new way. BCI describes the pulse oximeter as cost effective; transportable with an internal rechargeable battery; and adaptable to clinical, home, and sleep environments. For more information from BCI, circle number 154 on the reader service card in this issue or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/

LATEX-FREE ET TUBE GUIDE. Polamedco Inc introduces the Flexette™Stylette, a latex-free endotracheal tube guide. Company literature describes the product as having a soft, flexible tip to minimize trauma and increase patient safety, excellent malleability to allow easy shaping and forming, and a spiral handle that simplifies length adjustment. Polamedco offers the tube guide in 4 sizes: pediatric, small adult, small adult to adult, and adult. For more information from Polamedco Inc, circle number 155 on the reader service card in this issue, or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/



RESPIRATORY TEST SYSTEM. Nellcor Puritan Bennett introduces Breathlab PTS. Corporate literature describes this system as an advanced respiratory test system for biomedical engineers designed to facilitate testing of ventilators and other respiratory devices. Nellcor Puritan Bennett said the heart of the system is the PTS 2000™Tester, which combines the functions of a tester, oxygen meter, and manometer into a small, lightweight unit that measures pressure, flow, volume, oxygen concentration, and barometric pressure. It can be used as a stand-alone tester or connected to a PC and used with BreathLab PTS software. For more information, circle number 156 on the reader service card in this issue, or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/

MULTI-GAS MONITORS. CEA Instruments Inc introduces the *Personal Surveyor* series of UL-approved pocket-size, multi-gas monitors. Company literature lists such standard features as one-button operation, electronic zeroing, and high contrast digital display of temperature, alarm settings and all STEL, TWA, maximum, minimum, and current gas readings. A miniature self-contained air pump, data logging software, and carrying case are available. For more information from CEA Instruments, circle number 157 on the reader service card in this issue or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/

The Official Journal of the American Association for Respiratory Care
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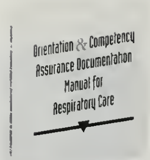


NEW! Orientation & Competency Manual

The Orientation and Competency Assurance Manual for Respiratory Care provides the information, assessment tools, and models necessary to demonstrate that the competence of employees is documented according to JCAHO requirements.

Item BK55 $65 ($90 nonmembers)

NEW! Uniform Reporting Manual for Subacute Care

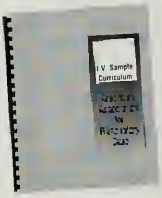
The Uniform Reporting Manual for Subacute Care is a tool to determine productivity, track trends in the utilization of respiratory care services, assist in determining personnel requirements, measure demand for and intensity of services, and meet the requirements of prospective payment systems. (PPS).

Item BK2 $75 ($115 nonmembers)

NEW! Respiratory Home Care Procedure Manual

The new Respiratory Home Care Procedure Manual is especially designed for the home care setting. And, it is easily adaptable to any alternate care site from subacute to home medical equipment companies and nursing agencies. The manual features five sections of information, forms, and checklists for the patient and practitioner.

Item BK3 $80 ($150 nonmembers)



NEW! I.V. Sample Curriculum

The I.V. Sample Curriculum is designed for use by respiratory care educational programs in conjunction with their clinical affiliates. A course following this curriculum will augment training programs for respiratory care practitioners with thorough instruction in I.V.-line placement and management. Contains everything needed to establish a complete I.V.-line course: lesson outlines, checklists and references.

Item BK18 $25 ($35 nonmembers)

Here's how to order —

Call the American Association for Respiratory Care at (972)243-2272

for your Continuing Education Needs

MEDWATCH

HE FDA MEDICAL PRODUCTS REPORTING PROGRAM

For VOLUNTARY reporting
by health professionals of adverse
events and product problems

Page ___ of ___

Form Approved OMB No. 0910-0291 Expires 4/30/96
See OMB statement on reverse

FDA Use Only (Resp Care)

Triage unit
sequence #

A. Patient information

. Patient identifier
In confidence

2. Age at time of event:
or
Date of birth:

3. Sex
☐ female
☐ male

4. Weight
___ lbs
or
___ kgs

B. Adverse event or product problem

. ☐ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)

Outcomes attributed to adverse event
(check all that apply)

☐ death ________ (mo/day/yr)
☐ life-threatening
☐ hospitalization – initial or prolonged
☐ disability
☐ congenital anomaly
☐ required intervention to prevent permanent impairment/damage
☐ other ________

Date of event (mo/day/yr)

4 Date of this report (mo/day/yr)

Describe event or problem

Relevant tests/laboratory data, including dates

Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

C. Suspect medication(s)

1 Name (give labeled strength & mfr/labeler, if known)
#1
#2

2 Dose, frequency & route used
#1
#2

3 Therapy dates (if unknown, give duration) from/to (or best estimate)
#1
#2

4 Diagnosis for use (indication)
#1
#2

5. Event abated after use stopped or dose reduced
#1 ☐ yes ☐ no ☐ doesn't apply
#2 ☐ yes ☐ no ☐ doesn't apply

6. Lot # (if known)
#1
#2

7. Exp. date (if known)
#1
#2

8. Event reappeared after reintroduction
#1 ☐ yes ☐ no ☐ doesn't apply
#2 ☐ yes ☐ no ☐ doesn't apply

9. NDC # (for product problems only)
– –

10. Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1. Brand name

2. Type of device

3 Manufacturer name & address

4. Operator of device
☐ health professional
☐ lay user/patient
☐ other:

5. Expiration date (mo/day/yr)

6.
model # ________
catalog # ________
serial # ________
lot # ________
other #

7. If implanted, give date (mo/day/yr)

8. If explanted, give date (mo/day/yr)

9. Device available for evaluation? (Do not send to FDA)
☐ yes ☐ no ☐ returned to manufacturer on ________ (mo/day/yr)

10 Concomitant medical products and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1. Name & address

phone #

2. Health professional?
☐ yes ☐ no

3. Occupation

4 Also reported to
☐ manufacturer
☐ user facility
☐ distributor

5. If you do NOT want your identity disclosed to the manufacturer, place an " X " in this box. ☐

Mail to: MEDWATCH
5600 Fishers Lane
Rockville, MD 20852-9787

or FAX to:
1-800-FDA-0178

A Form 3500 1/96)

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

ADVICE ABOUT VOLUNTARY REPORTING

Report experiences with:

- medications (drugs or biologics)
- medical devices (including in-vitro diagnostics)
- special nutritional products (dietary supplements, medical foods, infant formulas)
- other products regulated by FDA

Report SERIOUS adverse events. An event is serious when the patient outcome is:

- death
- life-threatening (real risk of dying)
- hospitalization (initial or prolonged)
- disability (significant, persistent or permanent)
- congenital anomaly
- required intervention to prevent permanent impairment or damage

Report even if:

- you're not certain the product caused the event
- you don't have all the details

Report product problems – quality, performance or safety concerns such as:

- suspected contamination
- questionable stability
- defective components
- poor packaging or labeling
- therapeutic failures

How to report:

- just fill in the sections that apply to your report
- use section C for all products except medical devices
- attach additional blank pages if needed
- use a separate form for each patient
- report either to FDA or the manufacturer (or both)

Important numbers:

• 1-800-FDA-0178	to FAX report
• 1-800-FDA-7737	to report by modem
• 1-800-FDA-1088	to report by phone or for more information
• 1-800-822-7967	for a VAERS form for vaccines

If your report involves a serious adverse event with a device and it occurred in a facility outside a doctor's office, that facility may be legally required to report to FDA and/or the manufacturer. Please notify the person in that facility who would handle such reporting.

Confidentiality: The patient's identity is held in strict confidence by FDA and protected to the fullest extent of the law. The reporter's identity, including the identity of a self-reporter, may be shared with the manufacturer unless requested otherwise. However, FDA will not disclose the reporter's identity in response to a request from the public, pursuant to the Freedom of Information Act.

The public reporting burden for this collection of information has been estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS Reports Clearance Office
Paperwork Reduction Project (0910-0291)
Hubert H Humphrey Building, Room 531-H
200 Independence Avenue, S W.
Washington, DC 20201

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Please do NOT return this form to either of these addresses.

U S DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service • Food and Drug Administration

FDA Form 3500-back

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Public Health Service
Food and Drug Administration
Rockville, MD 20857

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The FDA Medical Products Reporting Program
Food and Drug Administration
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American Association for Respiratory Care

MEMBERSHIP APPLICATION

Please read the eligibility requirements for each of the classifications in the right-hand column, then complete the applicable section. All information requested below must be provided, except where indicated as optional. See other side for more information and fee schedule. Please sign and date application on reverse side and type or print clearly. Processing of application takes approximately 15 days.

- ☐ Active
- Associate
  - ☐ Foreign
  - ☐ Physician
  - ☐ Industrial
- ☐ Special
- ☐ Student

Last Name ______________________________

First Name ______________________________

Social Security No. ______________________________

Home Address ______________________________

City ______________________________

State ____________ Zip __ __ __ __ __ — __ __ __ __

Phone No. (________) ______________________________

Primary Job Responsibility (check one only)

- ☐ Technical Director
- ☐ Assistant Technical Director
- ☐ Pulmonary Function Specialist
- ☐ Instructor/Educator
- ☐ Supervisor
- ☐ Staff Therapist
- ☐ Staff Technician
- ☐ Rehabilitation/Home Care
- ☐ Medical Director
- ☐ Sales
- ☐ Student
- ☐ Other, specify ______________________________

Type of Business

- ☐ Hospital
- ☐ Skilled Nursing Facility
- ☐ DME/HME
- ☐ Home Health Agency
- ☐ Educational Institution
- ☐ Manufacturer or supplier
- ☐ Other, specify ______________________________

Date of Birth (optional) ______________ Sex (optional) ____________

U.S. Citizen? _____ Yes _____ No

Have you ever been a member of the AARC? ______________________________

If so, when? From ______________ to ______________

Preferred mailing address: ☐ Home ☐ Business

For office use only

FOR ACTIVE MEMBER

An individual is eligible if he/she lives in the U.S. or its territories or was an Active Member prior to moving outside its borders or territories, and meets ONE of the following criteria: (1) is legally credentialed as a respiratory care professional if employed in a state that mandates such, OR (2) is a graduate of an accredited educational program in respiratory care, OR (3) holds a credential issued by the NBRC An individual who is an AARC Active Member in good standing on December 8, 1994, will continue as such provided his/her membership remains in good standing

PLEASE USE THE ADDRESS OF THE LOCATION WHERE YOU PERFORM YOUR JOB, NOT THE CORPORATE HEADQUARTERS IF IT IS LOCATED ELSEWHERE.

Place of Employment ______________________________

Address ______________________________

City ______________________________

State ____________ Zip __ __ __ __ __ - __ __ __ __

Phone No. (________) ______________________________

Medical Director/Medical Sponsor ______________________________

FOR ASSOCIATE OR SPECIAL MEMBER

Individuals who hold a position related to respiratory care but do not meet the requirements of Active Member shall be Associate Members. They have all the rights and benefits of the Association except to hold office, vote, or serve as chair of a standing committee The following subclasses of Associate Membership are available: Foreign, Physician, and Industrial (individuals whose primary occupation is directly or indirectly devoted to the manufacture, sale, or distribution of respiratory care equipment or supplies). Special Members are those not working in a respiratory care-related field

PLEASE USE THE ADDRESS OF THE LOCATION WHERE YOU PERFORM YOUR JOB, NOT THE CORPORATE HEADQUARTERS IF IT IS LOCATED ELSEWHERE.

Place of Employment ______________________________

Address ______________________________

City ______________________________

State ____________ Zip __ __ __ __ __ - __ __ __ __

Phone No. (________) ______________________________

FOR STUDENT MEMBER

Individuals will be classified as Student Members if they meet all the requirements for Associate Membership and are enrolled in an educational program in respiratory care accredited by, or in the process of seeking accreditation from, an AARC-recognized agency

SPECIAL NOTICE — Student Members do not receive Continuing Respiratory Care Education (CRCE) transcripts Upon completion of your respiratory care education, continuing education credits may be pursued upon your reclassification to Active or Associate Member

School/RC Program ______________________________

Address ______________________________

City ______________________________

State ____________ Zip __ __ __ __ __ - __ __ __ __

Phone No. (________) ______________________________

Length of program

- ☐ 1 year
- ☐ 2 years
- ☐ 4 years
- ☐ Other, specify ______________

Expected Date of Graduation *(REQUIRED INFORMATION)*

Month ________ Year ________

American Association for Respiratory Care • 11030 Ables Lane • Dallas, TX 75229-4593 • [972] 243-2272 • Fax [972] 484-2720

American Association for Respiratory Care MEMBERSHIP APPLICATION

Demographic Questions

We request that you answer these questions in order to help us design services and programs to meet your needs.

Check the Highest Degree Earned

- ☐ High School
- ☐ RC Graduate Technician
- ☐ Associate Degree
- ☐ Bachelor's Degree
- ☐ Master's Degree
- ☐ Doctorate Degree

Number of Years in Respiratory Care

- ☐ 0-2 years
- ☐ 3-5 years
- ☐ 6-10 years
- ☐ 11-15 Years
- ☐ 16 years or more

Job Status

- ☐ Full Time
- ☐ Part Time

Credentials

- ☐ RRT
- ☐ CRTT
- ☐ Physician
- ☐ CRNA
- ☐ RN
- ☐ LVN/LPN
- ☐ CPFT
- ☐ RPFT
- ☐ Perinatal/Pediatric

Salary

- ☐ Less than $10,000
- ☐ $10,001-$20,000
- ☐ $20,001-$30,000
- ☐ $30,001-$40,000
- ☐ $40,000 or more

PLEASE SIGN

I hereby apply for membership in the American Association for Respiratory Care and have enclosed my dues. If approved for membership in the AARC, I will abide by its bylaws and professional code of ethics. I authorize investigation of all statements contained herein and understand that misrepresentations or omissions of facts called for is cause for rejection or expulsion.

A yearly subscription to RESPIRATORY CARE journal and *AARC Times* magazine includes an allocation of $11.50 from my dues for each of these publications.

NOTE: Contributions or gifts to the AARC are not tax deductible as charitable contributions for income tax purposes. However, they may be tax deductible as ordinary and necessary business expenses subject to restrictions imposed as a result of association lobbying activities. The AARC estimates that the nondeductible portion of your dues — the portion which is allocable to lobbying — is 26%.

Signature ______________________________

Date ______________________________

Membership Fees

Payment must accompany your application to the AARC. Fees are for 12 months. (NOTE: Renewal fees are $75.00 Active, Associate-Industrial or Associate-Physician, or Special status; $90.00 for Associate-Foreign status; and $45.00 for Student status).

☐ Active	$ 87.50
☐ Associate (Industrial or Physician)	$ 87.50
☐ Associate (Foreign)	$102.50
☐ Special	$ 87.50
☐ Student	$ 45.00
TOTAL	$__________

Specialty Sections

Established to recognize the specialty areas of respiratory care, these sections publish a bi-monthly newsletter that focuses on issues of specific concern to that specialty. The sections also design the specialty programming at the national AARC meetings.

☐ Adult Acute Care Section	$15.00
☐ Education Section	$20.00
☐ Perinatal-Pediatric Section	$15.00
☐ Diagnostics Section	$15.00
☐ Continuing Care-Rehabilitation Section	$15.00
☐ Management Section	$20.00
☐ Transport Section	$15.00
☐ Home Care Section	$15.00
☐ Subacute Care Section	$15.00
TOTAL	$__________

GRAND TOTAL = Membership Fee plus optional sections $__________

- ☐ Total Amount Enclosed/Charged $__________________
- ☐ Please charge my dues (see below)

To charge your dues, complete the following:

- ☐ MasterCard
- ☐ Visa

Card Number

__ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __

Card Expires _______/______

Signature ________________________________

Mail application and appropriate fees to:
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Manuscript Preparation Guide

General Information

RESPIRATORY CARE welcomes original manuscripts related to the science and technology of respiratory care and prepared according to these Instructions and the *Uniform Requirements for Manuscripts Submitted to Biomedical Journals* [Respir Care 1997; 42(6):623-634]. Manuscripts are blinded and reviewed by professionals who are experts in their fields. Authors are responsible for all aspects of the manuscript and receive galleys to proofread before publication. Each accepted manuscript is copyedited so that its message is clear and it conforms to the Journal's style. Published papers are copyrighted by Daedalus Inc and may not be published elsewhere without permission.

Editorial consultation is available at any stage of planning or writing. On request, specific guidance is provided for all publication categories. To receive these Instructions and related materials, write to RESPIRATORY CARE, 600 Ninth Avenue, Suite 702, Seattle WA 98104, call (206) 223-0558, or fax (206) 223-0563.

Publication Categories & Structure

Research Article: A report of an original investigation (a study). It includes a Title Page, Abstract, Introduction, Methods, Results, Discussion, Conclusions, Product Sources, Acknowledgments, References, Tables, Appendices, Figures, and Figure Captions.

Evaluation of Device/Method/Technique: A description and evaluation of an old or new device, method, technique, or modification. It has a Title Page, Abstract, Introduction, Description of Device/Method/Technique, Evaluation Methods, Evaluation Results, Discussion, Conclusions, Product Sources, Acknowledgments, References, Tables, Appendices, Figures, and Figure Captions. Comparative cost data should be included wherever possible.

Case Report: A report of a clinical case that is uncommon, or was managed in a new way, or is exceptionally instructive. All authors must be associated with the case. A case-managing physician must either be an author or furnish a letter approving the manuscript. Its components are Title Page, Abstract, Introduction, Case Summary, Discussion, References, Tables, Figures, and Figure Captions.

Review Article: A comprehensive, critical review of the literature and state-of-the-art summary of a pertinent topic that has been the subject of at least 40 published research articles. Title Page, Outline, Introduction, Review of the Literature, Summary, Acknowledgments, References, Tables, Appendices, and Figures and Captions may be included.

Overview: A critical review of a pertinent topic that has fewer than 40 published research articles.

Update: A report of subsequent developments in a topic that has been critically reviewed in this Journal or elsewhere.

Point-of-View Paper: A paper expressing personal but substantiated opinions on a pertinent topic. Title Page, Text, References, Tables, and Illustrations may be included.

Special Article: A pertinent paper not fitting one of the foregoing categories may be acceptable as a Special Article. Consult with the Editor before writing or submitting such a paper.

Editorial: A paper drawing attention to a pertinent concern; it may present an opposing opinion, clarify a position, or bring a problem into focus.

Letter: A signed communication, marked "For publication," about prior publications in this Journal or about other pertinent topics. Tables and illustrations may be included.

Blood Gas Corner: A brief, instructive case report involving blood gas values—with Questions, Answers, and Discussion.

Drug Capsule: A mini-review paper about a drug or class of drugs that includes discussions of pharmacology, pharmacokinetics, and pharmacotherapy.

Graphics Corner: A brief case report incorporating waveforms for monitoring or diagnosis—with Questions, Answers, and Discussion.

Kittredge's Corner: A brief description of the operation of respiratory care equipment—with information from manufacturers and editorial comments and suggestions.

PFT Corner: Like Blood Gas Corner, but involving pulmonary function tests.

Cardiorespiratory Interactions. A case report demonstrating the interaction between the cardiovascular and respiratory systems. It should be a patient-care scenario; however, the case—the central theme—is the systems interaction. CRI is characterized by figures, equations, and a glossary. See the March 1996 Issue of RESPIRATORY CARE for more detail.

Test Your Radiologic Skill: Like Blood Gas Corner, but involving pulmonary medicine radiography and including one or more radiographs; may involve imaging techniques other than conventional chest radiography.

Review of Book, Film, Tape, or Software: A balanced, critical review of a recent release.

Preparing the Manuscript

Print on one side of white bond paper, 8.5 in. x 11 in. (216 x 279 mm) with margins of at least 1 in. (25 mm) on all sides of the page. Use *double-spacing* throughout the *entire* manuscript. Use a standard font (eg, Times, Helvetica, or Courier) at least 10 points in size, and do not use italics except for special emphasis. Number all pages in upper-right corners. Indent paragraphs 5 spaces. Do *not justify*. **Do *not* put authors' names, institutional affiliations or allusions to institutional affiliations in the text, or other identification anywhere except on the title page.** Repeat title only (no authors) on the abstract page. Begin each of the following on a new page: Title Page, Abstract, Text, Product Sources List, Acknowledgments, References, each Table, and each Appendix. Use standard English in the first person and active voice.

Center main section headings on the page and type them in capital and small letters (eg, Introduction, Methods, Results, Discussion). Begin subheadings at the left margin and type them in capital and small letters (eg, Patients, Equipment, Statistical Analysis).

References. Cite only published works as references. Manuscripts accepted but not yet published may be cited as references: designate the accepting journal, followed by (in press), and provide 3 copies of the in-press article for reviewer inspection. Cite references in the text with superscript numerals. Assign numbers in the order that references are first cited. On the reference page, list the cited works in numerical order. Follow the Journal's style for references. Abbreviate journal names as in *Index Medicus*. List all authors.

Article in a journal carrying pagination throughout volume:

> Rau JL, Harwood RJ. Comparison of nebulizer delivery methods through a neonatal endotracheal tube: a bench study. Respir Care 1992;37(11):1233-1240.

Article in a publication that numbers each issue beginning with Page 1:

> Bunch D. Establishing a national database for home care. AARC Times 1991;15(Mar):61,62,64.

Corporate author journal article:

> American Association for Respiratory Care. Criteria for establishing units for chronic ventilator-dependent patients in hospitals. Respir Care 1988;33(11):1044-1046.

Article in journal supplement: (Journals differ in their methods of numbering and identifying supplements. Supply sufficient information to promote retrieval.)

> Reynolds HY. Idiopathic interstitial pulmonary fibrosis. Chest 1986; 89(3 Suppl):139S-143S.

Abstract in journal: (Abstracts citations are to be avoided. Those more than 3 years old should not be cited.)

> Stevens DP. Scavenging ribavirin from an oxygen hood to reduce environmental exposure (abstract). Respir Care 1990;35(11): 1087-1088.

Editorial in journal:

> Enright P. Can we relax during spirometry? (editorial). Am Rev Respir Dis 1993;148(2):274.

Editorial with no author given:

> Negative-pressure ventilation for chronic obstructive pulmonary disease (editorial). Lancet 1992;340(8833):1440-1441.

Letter in journal:

> Aelony Y. Ethnic norms for pulmonary function tests (letter). Chest 1991;99(4):1051.

Paper accepted but not yet published:

> Hess D. New therapies for asthma. Respir Care (year, in press).

Personal author book: (For any book, specific pages should be cited whenever possible.)

> DeRemee RA. Clinical profiles of diffuse interstitial pulmonary disease. New York: Futura; 1990. p. 76-85.

Corporate author book:

> American Medical Association Department of Drugs. AMA drug evaluations. 3rd ed. Littleton CO: Publishing Sciences Group; 1977.

Chapter in book with editor(s):

> Pierce AK. Acute respiratory failure. In: Guenter CA. Welch MH, editors. Pulmonary medicine. Philadelphia: JB Lippincott; 1977:26-42.

Tables. Use consecutively numbered tables to display information. Start each table on a separate page. Number and title the table and give each column a brief heading. Place explanations in footnotes, including all nonstandard abbreviations and symbols. Key the footnotes with conventional designations (*, †, ‡, §, ||, ¶, **, ††) in consistent order, placing them superscript in the table body. Do not use horizontal or vertical rules or borders. Do not submit tables as photographs, reduced in size, or on oversize paper. Use the same typeface as in the text.

Illustrations. Graphs, line drawings, photographs, and radiographs are figures. Use only illustrations that clarify and augment the text. Number them consecutively as Fig. 1, Fig. 2, and so forth according to the order by which they are mentioned in the text. Be sure all figures are cited. If any figure was previously published, include copyright holder's written permission to reproduce. Figures for publication must be of professional quality. Data for the original graphs should be available to the Editor upon request. If color is essential, consult the Editor for more information. In reports of animal experiments, use schematic drawings, not photographs. A letter of consent must accompany any photograph of a person. Do not place titles and detailed explanations on figures; put this information in figure captions. If possible, submit radiographs as prints and full-size copies of film.

Drugs. Identify precisely all drugs and chemicals used, giving generic names, doses, and routes of administration. If desired, brand names may be given in parentheses after generic names. Drugs should be listed on the product-sources page.

Commercial Products. In parentheses in the text, identify any commercial product (including model number if applicable) the first time it is mentioned, giving the manufacturer's name, city, and state or country. If four or more products are mentioned, do not list any manufacturers in the text; instead, list them on a Product Sources page at the end of the text, before the References. Provide model numbers when available and manufacturer's suggested price, if the study has cost implications.

Ethics. When reporting experiments on human subjects, indicate that procedures were conducted in accordance with the ethical standards of the *World Medical Association Declaration of Helsinki* [Respir Care 1997;42(6):635-636] or of the institution's committee on human experimentation. State that informed consent was obtained. Do not use patient's names, initials, or hospital numbers in text or illustrations. When reporting experiments on animals, indicate that the institution's policy, a national guideline, or a law on the care and use of laboratory animals was followed.

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Units of Measurement. Express measurements of length, height, weight, and volume in metric units appropriately abbreviated; temperatures in degrees Celsius; and blood pressures in millimeters of mercury (mm Hg). Report hematologic and clinical-chemistry measurements in conventional metric and in SI (*Systémé Internationale*) units. Show gas pressures (including blood gas tensions) in torr. List SI equivalent values, when possible, in brackets following non-SI values—for example, "PEEP, 10 cm H_2O [0.981 kPa]." For conversion to SI, see RESPIRATORY CARE 1988;33(10):861-873 (Oct 1988), 1989;34(2):145 (Feb 1989), and 1997;42(6):639-640 (June 1997).

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Submitting the Manuscript

Mail three copies [1 copy with author(s) name(s), affiliation(s), 2 copies without name(s) and affiliation(s) for reviewers] of the manuscript, figures, and 1 diskette, and the Cover Letter & Checklist to RESPIRATORY CARE, 600 Ninth Avenue, Suite 702, Seattle WA 98104. Do not fax manuscripts. Protect figures with cardboard. Keep a copy of the manuscript and figures. Receipt of your manuscript will be acknowledged.

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Author Signature/Date ____________________

*Fourth Author: ____________________

Author Signature/Date ____________________

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Calendar of Events

AARC & AFFILIATES

October 1—*Boise, Idaho*

The Idaho Society for Respiratory Care will hold its annual education meeting at the Double Tree Riverside in Boise. The morning session will consist of lectures on management of the difficult airway, graphic waveform analysis, sleep medicine, and new aerosol delivery devices. The afternoon session will include hands-on break out sessions on waveform analysis, intra-pulmonary percussive ventilation, and the basics of chest CTs.

Contact: Jeff Anderson at (208) 385-3674.

October 6—*Live Broadcast*

Participate in a live, fully interactive, 90-minute satellite broadcast of the eighth installment of the AARC's 1998 "Professor's Rounds" series. "Techniques for Weaning the Ventilator Patient" will be broadcast from 12:30–2 p.m. (EST) and features Dean R Hess PhD RRT and Richard D Branson BS RRT.

CRCE: 1 credit hour

Contact: The AARC at (972) 243-2272.

October 7–9—*Worthington, Ohio*

The OSRC will be conducting its 22nd annual meeting at the Holiday Inn in Worthington. A variety of current topics will be discussed along with specialty sessions in management and education.

CRCE: AARC CRCE credits will be available.

Contact: Dan Wine, Grady Memorial Hospital, 561 W Central Ave, Delaware OH 43015 or call (614) 368-5315.

October 8—*New York Society, Southeastern Chapter*

30th Annual Symposium at the Marriott Marquis in Manhattan, New York. AARC Executive Director Sam Giordano MBA RRT will speak on "The RCP: Practice in the 21st Century." Also, the NYSSRC and SUNY Stony Brook will be hosting a clinical assessment workshop Oct. 9-10 at the Cornell Club in Manhattan.

Contact: (516) 444-3181 or www.nyssrc.org

October 9—*Colorado Society, Southern Chapter*

5th Annual Southern Colorado Pulmonary Symposium at the Holiday Inn Garden of the Gods, Colorado Springs, Colorado.

Contact: Cathy Fletchall at (719) 776-5025 or Barry Beard at (719) 776-5212.

October 17—*Anchorage, Alaska*

The Alaska Society for Respiratory Care will present its "Fall Lung Conference and Meeting" at Providence Anchorage Medical Center. Speakers include Dennis Bing RRT and Mark Siobal RRT. Sponsored by the ASRC, Dräger, Nellcor Puritan Bennett, and Sensormedics.

Contact: Wayne Wallace BA RRT at (907) 486-9517 or e-mail wwallace@ptialaska.net.

October 20—*Videotape Teleconference*

After viewing a tape of the seventh installment of the AARC's 1998 "Professor's Rounds" series, "Assess and Treat Protocols," participate in a live telephone question-and-answer session with the expert (from 12:30–1 pm EST). Judith Tietsort RN RRT will discuss getting physician buy-in, getting started, preparing your staff, and measuring outcomes.

CRCE: One credit hour

Contact: To receive the 90-minute videotape and register for the teleconference, call the AARC at (972) 243-2272.

November 7–10—*International Respiratory Congress, Atlanta, Georgia*

The American Association for Respiratory Care hosts its 44th annual International Respiratory Congress at the Georgia World Congress Center in Atlanta, GA. More than 7,000 people will experience programs appealing to all levels of health care providers — from clinicians to managers and administrators, to manufacturers and distributors of equipment and supplies. Program content will include neonatal, pediatric, and adult critical care; acute, continuing, and rehabilitative care; diagnostics; management; and case and disease management — truly a comprehensive program on respiratory care. Exhibits by all manufacturers of cardiopulmonary equipment in the world will be featured.

Contact: For program brochure and registration information, contact the AARC at 11030 Ables Lane, Dallas, TX 75229-4593; (972) 243-2272; fax (972) 484-2720; meetings@aarc.org; or www.aarc.org.

November 17—*Videotape Teleconference*

After viewing a tape of the eighth installment of the AARC's 1998 "Professor's Rounds" series, "Techniques for Weaning the Ventilator Patient," participate in a live telephone question-and-answer session with the expert (from 12:30–1 pm EST). Dean R Hess PhD RRT will analyze the pros and cons both inside and outside the hospital.

CRCE: One credit hour.

Contact: To receive the 90-minute videotape and register for the teleconference, call the AARC at (972) 243-2272.

Other Meetings

June12-16, 1999—*International Society for Aerosols in Medicine*

12th International Congress at the Austria Center in Vienna, Austria

Contact: Vienna Academy of Postgraduate Medical Education and Research. Alser Strasse 4, A-1090 Vienna, Austria. Phone (+43/1) 405 13 83-22, fax (+43/1) 405 13 83-23, e-mail medacad@via.at.

Notices

Notices of competitions, scholarships, fellowships, examination dates, new educational programs, and the like will be listed here free of charge. Items for the Notices section must reach the Journal 60 days before the desired month of publication (January 1 for the March issue, February 1 for the April issue, etc). Include all pertinent information and mail notices to RESPIRATORY CARE Notices Dept, 11030 Ables Lane, Dallas TX 75229-4593.

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ATLANTA, GEORGIA

1998

Helpful Web Sites

American Association for Respiratory Care
http://www.aarc.org
- Current job listings
- American Respiratory Care Foundation fellowships, grants, & awards
- Clinical Practice Guidelines

National Board for Respiratory Care
http://www.nbrc.org

RESPIRATORY CARE online
http://www.rcjournal.com
- 1997 Subject and Author Indexes
- Contact the editorial staff

The American College of Chest Physicians
http://www.chestnet.org

The National Board for Respiratory Care—1999 Examination Dates and Fees

Examination	Examination Date	Examination Fee	
CRT Examination	March 13, 1999 Application Deadline: January 1, 1999	$120 80	(new applicant) (reapplicant)
RRT Examination	June 5, 1999 Application Deadline: February 1, 1999	120 80	written only (new applicant) written only (reapplicant)
CPFT Examination	June 5, 1999 Application Deadline. April 1, 1999	130 150	(new applicant) (reapplicant)

For information about other services or fees, write to the National Board for Respiratory Care, 8310 Nieman Road, Lenexa KS 66214, or call (913) 599-4200, FAX (913) 541-0156,or e-mail: nbrc-info@nbrc.org

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New *Federal Register* Notices Now Available

The Center for Devices and Radiological Health announces the publication of new Facts-on-Demand FOD notices in the *Federal Register*. The new publications: FOD#774—Medical Devices; Preemption of State Product Liability Claims; Proposed Rule; FOD#607—Rebuilders, Reconditioners, Services, and "As Is" Remarketers of Medical Devices; Review and Revision of Compliance Policy Guides and Regulatory Requirements; Request for Comments and Information; Proposed Rule; and FOD#513—Medical Devices; Reports of Corrections and Removals; Stay of Effective Date of Information Collection Requirements; Stay of Effective Date of Final Regulation. For more information about Facts-on-Demand call (800) 899-0381 or (301) 826-0111. The FOD system is also on the Internet at www.fda.gov/cdrh/fedregin.html.

NAMES 1998 Education, Conference Schedule Set

The National Association for Medical Equipment Services (NAMES) announces its 1998 national conferences and regional education seminars. For information about upcoming events, call the NAMES Education & Meeting Department at (703) 836-6263, or visit the web site: www.names.org.

Web Site Link to Fellowships, Scholarships, & Grants

The American Association for Respiratory Care's web site contains important information about fellowships, scholarships, and research grants. International fellowships, education scholarships, research fellowships, and other grand programs are described in detail. The site also contains information about the $1,000,000 Research Fund, a restricted fund to sponsor research initiatives that document the clinical and economic impact of respiratory care professionals in the delivery of health care. To apply, a "Research Plan Abstract" must be submitted to the AARC by February 1, 1999. To find out more about these programs, log on at **www.aarc.org.**

Year 2000 Date Problem Addressed by FDA

On June 24, 1998, the Food and Drug Administration announced the availability of the document, "Guidance on FDA's Expectations of Medical Device Manufacturers Concerning the Year 2000 Date Problem." The document is available via telephone (800) 899-0381 or (301) 827-0111 or via the Internet at www.fda.gov/cdrh/yr2000/y2kguide.html.

New Address for Asthma Group

The Allergy and Asthma Network Mothers of Asthmatics Inc has moved. The organization's new address is 2751 Prosperity Avenue, Suite 150, Fairfax VA 22031. The telephone numbers are (800) 878-4403 or (703) 641-9595, Fax (703) 573-7794. Information about the group and their activities is available at their Internet address: www.aanma.org.

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SUBSCRIPTION RATES FOR ASSOCIATIONS. Basic annual subscriptions are offered to members of associations according to their membership enrollment: 101-500 members = $13.50/year; 501-1,500 = $13/year; 1,500-10,000 = $12.50/year; more than 10,000 = $11.50/year. Individual subscriptions ar available at these rates: $75/year (12 issues in the United States or Puerto Rico; $90/year in other countries. For information, contact Ray Masferrer at (972) 243-2272.

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MANUSCRIPTS. The Journal publishes clinical studies, method/device evaluations, reviews, and other materials related to cardiopulmonary medicine and research. Manuscripts may be submitted to the Editorial Office, RESPIRATORY CARE, 600 Ninth Avenue, Suite 702, Seattle WA 98104. Instructions for authors are printed in every issue. An expanded version of the Instructions is available from the editorial office.

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